IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, and ENDO PAR INNOVATION COMPANY, LLC,	)	
Plaintiffs,	)	C.A. No. 18-823-CFC
v.	)	**FILED UNDER SEAL**
EAGLE PHARMACEUTICALS INC.,	)	
Defendant.	)	

JOINT CLAIM CONSTRUCTION BRIEF

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A. PAR'S OPENING STATEMENT

1. Background

This is a Hatch-Waxman case in which Plaintiffs Par Pharmaceutical, Inc., Par Sterile Products, LLC, and Par Innovation Company, LLC (collectively, "Par") assert claims for infringement of six patents,[1] arising out Defendant Eagle Pharmaceutical Inc.'s ("Eagle") submission of an ANDA seeking FDA approval to engage in the commercial manufacture and sale of a proposed generic version of Par's VASOSTRICT® products prior to the expiration of Par's patents.

The active ingredient in VASOSTRICT® is vasopressin, a synthetic polypeptide used to raise a patient's blood pressure, in part, by constricting blood vessels throughout the body. Certain illnesses, such as sepsis (a life-threatening complication of an infection), can result in dangerously low blood pressure due to dilation of blood vessels (among other things). Vasopressin, together with other interventions, may be used to return a patient's blood pressure to less dangerous

[1] The patents-in-suit are U.S. Patent Nos. 9,375,478 ("'478 patent"), 9,744,239 ("'239 patent"), 9,687,526 ("'526 patent"), 9,750,785 ("'785 patent"), 9,744,209 ("'209 patent"), and 9,937,223 (the "'223 patent"). They are all from the same patent family, and are continuations or continuations-in-part from the same ultimate parent application (US Application No. 14/610,499). There is therefore substantial overlap amongst the specifications of each patent.

levels. *See, e.g.,* '239 patent (Ex. 1), col. 1:21-28, 2:1-32, 3:39-5:43, 24:15-19; Coralic Decl. (Ex. 20), ¶ 4.

The patentees do not claim to have invented vasopressin itself. Instead, the patents-in-suit teach and claim vasopressin formulations that have enhanced stability and lower impurity levels as compared to those of prior art vasopressin formulations. One of the difficulties associated with developing such formulations is that vasopressin degrades (breaks down) in aqueous solutions, which gets worse over time. *See, e.g.,* '209 patent (Ex. 4), col. 3:23-4:40. As is described throughout the specifications, the patentees undertook extensive work to identify, characterize, and quantify various vasopressin degradants and the extent of vasopressin degradation, including by measuring how the levels of vasopressin and various vasopressin degradation products change over time and vary with different formulations. *Id.*, col. 3:23-4:40; 52:5-116:45.

Historically, vasopressin products have been sold as injectable products that were packaged in vials and intended for intravenous administration. Coralic Decl. (Ex. 20), ¶ 12. Vasopressin is administered in almost all instances via continuous intravenous administration using an IV drip, in which the vasopressin is diluted before use. Though there are exceptions to that, they are exceedingly rare—they are only administered without dilution when a patient has no pulse. *Id.*, ¶¶ 13-15.

2. Summary of Argument

The disputed claim limitations are comprised of readily-understandable are used in accord with their ordinary meaning to skilled artisans. The nature of the parties' disputes is readily apparent from Eagle's proposed constructions, each of which seeks to restrict the term's ordinary meaning in improper ways. In view of the nature of the parties' disputes, there is no reason for the Court to try to re-state using different words the meaning of claim terms that are already understood. Thus, the Court need not provide specific constructions for those terms, beyond confirming that they are each to be given their ordinary meaning and rejecting Eagle's attempts to impose unwarranted restrictions on those meanings. *See, e.g., Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1291 (Fed. Cir. 2015) (noting the term at issue "is comprised of commonly used terms; each is used in common parlance and has no special meaning in the art," and "[b]ecause the plain and ordinary meaning of the disputed claim language is clear, the district court did not err by declining to construe the claim term").[2]

[2] *See also, e.g., Mentor H/S, Inc. v. Medical Device Alliance, Inc.*, 244 F.3d 1365, 1380 (Fed. Cir. 2001) ("The defendants argue that the court committed reversible error by refusing to construe the claim terms 'irrigating' and 'frictional heat.' Mentor argues that the court properly instructed the jury that these terms should receive their ordinary meanings. We agree with Mentor that the district court did not err in relying on the ordinary meanings of these terms."); *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1326 (Fed. Cir. 2012) ("[t]he district court did not err in concluding that these terms have plain meanings that do not require additional construction"); and "ActiveVideo's proposed

Each of Eagle's proposed constructions seeks to impermissibly restrict the ordinary meaning of the disputed terms. Federal Circuit precedent is clear, however, that such narrowing constructions are appropriate in only two circumstances: (1) where the patentee acts as his own lexicographer and clearly defines the term in question; and (2) where the patent and/or prosecution history provides an unmistakable disavowal of claim scope. *See, e.g., Hill-Rom Services, Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014); *Thorner v. Sony Computer Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012); *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 805 F.3d 1368, 1375-76 (Fed. Cir. 2015).[3] Neither exception applies to the terms at issue here, and Eagle cannot overcome the heavy presumption that those terms are to be afforded their ordinary meaning. *See Aventis Pharms. Inc. v. Amino Chems. Ltd.*, 715 F.3d 1363, 1373 (Fed. Cir. 2013) ("There is a heavy presumption that claim terms are to be given their ordinary and customary meaning.").

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construction erroneously reads limitations into the claims and the district court properly rejected that construction and resolved the dispute between the parties.").

[3] *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (absent lexicography or disavowal, claim terms are to be given their "ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question ["POSA"] at the time of the invention").

B. EAGLE'S ANSWERING STATEMENT

1. Background

Vasopressin is a drug that has been in use for almost a century, first introduced to the market by Parke-Davis in the 1920s. *See* Ex. 23 (FDA Clinical Pharmacology Review of NDA No. 204-485 ("FDA NDA Review")) at EAGLEVAS0014308.[4] Because the drug was introduced to the market before the FDA introduced its modern drug review protocol, it was sold and used only as a generic drug, without FDA approval, for decades. *See id.* at EAGLEVAS0014305.

Due to the length of the drug's use, there is an extensive body of literature covering virtually every aspect of vasopressin. Indeed, when Par submitted a New Drug Application ("NDA") for its proposed vasopressin formulation in 2012, it did so relying ***entirely on prior art literature*** to support its application, rather than any clinical trial data from Par. *See* FDA NDA Review at EAGLEVAS0014305. Notably, the FDA determined that Par's proposed vasopressin formulation—also the subject matter of the patents-in-suit—"***is not significantly different***" from the prior art formulations, and subsequently approved Par's application. *See* Ex. 23 (Biopharmaceutics Review: NDA 204485 ("FDA Biopharmaceutics Review")) at EAGLEVAS0014354.

[4] JHP Pharmaceuticals was acquired by Par subsequent to submission of NDA No. 204485.

When Par was before the Patent Office to secure patents for its vasopressin formulation, however, the extensive body of literature worked against Par, and Par needed to make fine distinctions against the prior art. As set forth below, those distinctions Par made before the Patent Office—which were dispositive to allowance of Par's patents on its vasopressin formulation—are now vigorously dismissed in Par's opening brief, under the guise of its "[o]rdinary meaning" constructions.

2. Introduction

By pressing its uninformative "[o]rdinary meaning" constructions for each of the disputed claim terms, Par is asking the Court to defer ruling on the parties' claim construction disputes until trial. Par's motivation is clear. It wants to keep this suit alive for as long as possible, knowing that its own statements—both in the asserted patents themselves and during prosecution—establish that Eagle's proposed ANDA product cannot infringe the asserted claims, as properly construed, as a matter of law. This runs afoul of Federal Circuit precedent, which states, "[a] determination that a claim term 'needs no construction' or has the 'plain and ordinary meaning' may be inadequate. . . when reliance on a term's 'ordinary' meaning does not resolve the parties' dispute." *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d

1351, 1361 (Fed. Cir. 2008).[5] Thus, Eagle respectfully requests that the Court construe all the terms set forth in this brief.

As noted above, Par's explanations of what it contends are the "ordinary meanings" of the disputed claim terms directly contradict arguments it made to the Patent Office to secure its patents. For example, to overcome a claim rejection during prosecution, Par argued that a prior art formulation with acetic acid for pH adjustment did not include an "acetate buffer" as claimed. [redacted]

Similarly, to overcome prior art that disclosed an almost identical vasopressin dosage form to that claimed but that did not explicitly state it could be diluted before administration, Par explicitly added a dilution step to the claims of the '239 patent. Par then argued—successfully—that a POSA would not have found it obvious to dilute the prior art formulation before administration. Now, relying heavily on extrinsic evidence, Par argues the opposite—that a POSA would know that such a

[5] *See also In re Mobile Telecomms. Techs., LLC*, 265 F.Supp. 3d 454, 467 (D. Del. 2017) ("Because . . . the term has more than one ordinary meaning, and the parties present a genuine dispute, a construction other than an unspecified plain and ordinary meaning is required.").

formulation must almost always be diluted before administration, even where a dilution step is not specified in the claims. Not only does Par's approach violate the core principle of claim construction that extrinsic evidence cannot be used to contradict the intrinsic record, *see*, *e.g.*, *Interactive Gift Express. Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1332 (Fed. Cir. 2001), but it also lays bare the fact that Par's "ordinary meaning" constructions cannot sufficiently delineate the scope of the claims in light of the intrinsic evidence.

Par's constructions are improper for another reason—they ignore the actual language of the claims. *See Interactive Gift Exp., Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001) ("In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves."). On the "administering" limitations, four of the asserted patents[6] recite a "unit dosage form" (or "pharmaceutical composition") having a specified concentration of vasopressin and pH, and provide that ***the*** "unit dosage form" (or "pharmaceutical composition") is administered. The plain and natural reading of these claims is that it is the unit dosage form described in the claims—with all of the recited properties—that must

[6] There are six patents asserted in this case: U.S. Patent Nos. 9,375,478 ("'478 patent"), 9,744,239 ("'239 patent"), 9,687,526 ("'526 patent"), 9,750,785 ("'785 patent"), 9,744,209 ("'209 patent"), and 9,937,223 (the "'223 patent"). One of the patents ('785 patent) is directed to a composition and thus does not include an administering limitation discussed for the remainder of the patents.

be administered to the patients. Once diluted, a unit dosage form takes on *different* properties for claimed parameters such as concentration and pH. Thus, once diluted, it is a *different* unit dosage form that is administered, *i.e.*, the "***diluted*** unit dosage form" in the words of the '239 patent. Under Par's apparent reading of the claims, the dilution step of the '239 patent, and the instruction to administer "the diluted unit dosage form"—claim elements specifically added to overcome prior art during prosecution—would improperly be rendered superfluous, as Par reads them into every claim regardless.

Finally, Par mischaracterizes the parentheticals in Eagle's constructions of the "acetate buffer" and "administering" terms as improperly adding limitations to the claims. To the contrary, Eagle included those explanatory parentheticals in order to crystalize the parties' known disputes before the Court and to provide a meaningful notice of its position to Par prior to briefing. As Par's own authority establishes, "the legal function of giving meaning to claim terms always takes place in the context of a specific accused infringing device or process" and "it is efficient to focus on the construction of only the disputed elements or limitations of the claims." *Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1326–27 (Fed. Cir. 2006); *see also, e.g.*, *Spectrum Pharm. Inc. v. InnoPharma, Inc.*, C.A. No. 12–260–RGA–CJB, 2014 WL 3365684, at *11 (D. Del. July 3, 2014). Now that the parties have a better understanding of the disputes before the Court, Eagle

respectfully submits that the claims may be construed without reference to these parentheticals, should the Court be inclined to do so. But in doing so, Eagle respectfully requests that the Court resolve the parties' disputes as reflected herein.

C. PAR'S REPLY STATEMENT

Eagle spends a lot of time talking about infringement and validity issues, neither of which is before the Court. Those issues are for another day, following discovery and the presentation of a full record on those issues.

On the issue presently before the Court—claim construction—there is no reason for the Court to deviate from the ordinary meaning of any of the three disputed claim terms:

- With respect to "vasopressin degradation products," the issue is whether the patentees acted as their own lexicographer so as to restrict the scope of the term for purposes of the claimed invention to a specified subset of all vasopressin degradants. They did not.
- With respect to "acetate buffer," the issue is whether the patentees made a clear and unequivocal disclaimer of claim scope during the prosecution of a patent related to the patents-in-suit. They did not.
- With respect to the disputed "administering" limitations, the issue is whether the patentees intended to exclude the preferred mode of

administration (continuous intravenous infusion via an IV drip) from the scope of the claims. They did not.

In each instance, Eagle bears a heavy burden to overcome the strong presumption in favor of construing those terms in accordance with their ordinary meaning. For the reasons discussed herein, Eagle cannot do so with respect to any of the three terms.

Moreover, with respect to all three disputed claim terms, Eagle relies on extrinsic evidence in the form of a declaration from an expert witness, Dr. Mansoor Amiji (*see* Ex. 25). For the most part, however, the declaration simply regurgitates the legal arguments Eagle raises in its answering brief, providing little if any scientific or technical information that would be helpful to the Court in construing those terms. He also opines about matters outside the scope of his expertise, such as the supposed grammatical implications of the patentees' use of the phrase "administering ***the*** [vasopressin] composition" when he is neither a linguist nor someone with experience concerning the use and administration of vasopressin compositions, and opines about the implications of prosecution history estoppel, when he is not a patent attorney. His declaration is of no use to the Court.

D. EAGLE'S SUR-REPLY STATEMENT

Par's arguments find their center in attorney argument and extrinsic evidence. First, Par seeks to run away from its lexicography regarding "vasopressin

degradation products." While Par might now wish it was more inclusive, the patent's definition remains limited to Table 1. And with good reason: without this definition, POSAs would not know which compounds to count in the 0-2% limit in the claims, rendering them indefinite.

For "acetate buffer," Par offers a strained reading of its prosecution statements, which clearly distinguished acetic acid for pH adjustment in the prior art. In doing so, Par relies on new opinions from Dr. Kirsch that directly contradict opinions he gave in an earlier case regarding ***the same term***. As Dr. Kirsch previously opined, acetic acid alone ***cannot*** form an "acetate buffer."

Finally, on the "administering" terms, Par's arguments rely on unsupported hypotheticals and speculation about what might have "made sense" for Par's business interests. But well-established precedent mandates that courts construe claims based on the language as written, not on what patentees wish they had written.

I. AGREED UPON CONSTRUCTIONS

The parties have agreed that the claim term "vasopressin" should be construed as "arginine vasopressin as described in SEQ. ID. NO. 1 (*see, e.g.*, '239 patent, cols. 25-26)" with respect to each of the patents-in-suit.

II. DISPUTED CONSTRUCTIONS

A. "VASOPRESSIN DEGRADATION PRODUCTS"

1. Par's Opening Position:

The term "vasopressin degradation products" appears in '239 claims 1 and 15. The parties' respective proposed constructions are as follows:

Par's Proposed Construction	**Eagle's Proposed Construction**
Ordinary meaning, no construction necessary	"The compounds listed in TABLE 1, having SEQ ID NOs. 2–17"[7]

As described above, the level of vasopressin degradants, and how they change over time, can be measured as a way of assessing a vasopressin formulation's long-term stability. The parties' dispute about the term "vasopressin degradation products" is not about the ordinary meaning of those words or the term as a whole, but is instead, whether that term should cover any vasopressin degradation products (Par's position), or just those degradants that are specifically listed in a particular table in the specification (Eagle's position). There is no basis to limit the term to just a subset of degradants as Eagle proposes, because Eagle cannot meet its heavy burden to show that the patentees either acted as their own lexicographer or disavowed claim scope with respect to this term.[8] Accordingly, the Court should adopt Par's proposal.

[7] A copy of Table 1 is cut and pasted as Attachment A hereto.

[8] To Par's knowledge, Eagle does not contend that Table 1 of the '239 patent lists all possible vasopressin degradation products, but contends instead that the

Nothing in the language of the claims themselves—which recite that the claimed vasopressin compositions consist of, among other things, "0-2% vasopressin degradation products"—suggests that the patentees intended to deviate from the term's ordinary meaning or otherwise limit it to just certain degradation products. Whereas some of the dependent claims of the '239 patent refer to particular degradation products by SEQ ID numbers (claims 2, 3, and 4),[9] independent claims 1 and 15 do not. If the patentees had intended those broader claims to likewise be limited to certain degradation products, they could have easily done so by, for example, reciting "0-2% of the degradation products of SEQ ID Nos. 2-17" (*i.e.*, those degradants specifically listed in Table 1). The fact that they did not do so evinces an intent that the term encompasses any vasopressin degradation products, not just particular ones.

Likewise, the '239 patent specification and file history contain no lexicography or disavowal limiting the plain meaning of "vasopressin degradation products." "[A] claim term is only given a special definition different from the term's plain and ordinary meaning if the 'patentee . . . clearly set[s] forth a definition

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patentees somehow intended to limit the scope of this term to just those particular degradants. The evidence they cite, however, does not support that conclusion.

[9] For example, '239 claim 2 depends from claim 1, and recites "wherein the vasopressin degradation products include SEQ ID NO.: 2, wherein SEQ ID NO.: 2 is present in the unit dosage form in an amount of about 0.01%."

of the disputed claim term other than its plain and ordinary meaning.' *Thorner*, 669 F.3d at 1365 (citations omitted). A patentee can also disavow claim scope, but the standard 'is similarly exacting.' *Id.* at 1366." *Akamai Techs, Inc. v. Limelight Networks, Inc.*, 805 F.3d 1368, 1375 (Fed. Cir. 2015).

With respect to the table cited in Eagle's proposed construction, for example, the specification states only that "[v]asopressin and associated degradation products or peptides are listed in Table 1 below." '239 patent (Ex. 1), at 3:1-3. Nothing in that description or elsewhere indicates that Table 1 is intended to define the scope of the term "vasopressin degradation products," or that the patentees intended to exclude any other degradants.[10]

Consistent therewith, Example 1 in the specification describes the analysis of degradation products of vasopressin that *can* be present in an *illustrative* formulation of vasopressin. *Id.* at 16:9-15 ("To analyze degradation products of vasopressin that can be present in an illustrative formulation of vasopressin, gradient HPLC was performed to separate vasopressin from related peptides and formulation components."). And in Table 3 within Example 1, the patentees identify a degradant not listed in Table 1—"Dimeric-vasopressin (Dimer-AVP)." This evidences that Table 1 is not inclusive of all vasopressin degradation products.

[10] The specification does not say, for example, that "vasopressin and the associated degradation products as used herein *are defined in* Table 1."

Then, Example 2 analyzes the effect of pH on the stability of vasopressin. In doing so, the studies assessed the degradation of vasopressin by measuring changes in the amount of vasopressin and total impurities over time. *See id.* at 19:45-20:5. By measuring *total* impurities, Example 2 does not address the identity of the degradation products or otherwise limit vasopressin degradation products to the particular degradants identified in Table 1.

In the parties' Joint Claim Construction Statement, Eagle cites nearly 100 pages of prosecution history, but does not point to any specific language that it contends might be an unequivocal disavowal of claim scope. There is no such disavowal.

Eagle cites, for example, to an August 2015 Office Action Response (Ex. 7) and accompanying Vandse Declaration (Ex. 8). As with the Examples from the specification discussed above, however, those documents discuss studies conducted on the stability of vasopressin formulations under a variety of conditions by measuring changes in the amount of vasopressin and the total amount of specified and unspecified impurities over time. *See, e.g.*, Ex. 7 at 8-9 (arguing that the claimed inventions "provide surprising and unexpected results over the state of the art" based upon the measured values of vasopressin and "% total impurities"); Ex 8 at 2-11. Nothing in the description of these studies or the reported results evinces an intent to limit the phrase "vasopressin degradation products" to just particular, specified

degradants. To the contrary, the Appendices to the Vandse Declaration report on the percentage amounts of a variety of "Related Substances," some of which are included on the list of degradants in Table 1 of the specification (i.e., "Gly9-AVP," "Glu4-AVP," "D-Asn-AVP," "ASP5-AVP," and "Acetyl-AVP") whereas others are not, including "AVP-Dimer" and a number of unidentified substances denominated "UI-____," along with a composite figure for "Total Impurities." Ex. 8 at 12-55.

Indeed, the term "vasopressin degradation products" is not used in either of these documents, and that term was not even recited in the claims being prosecuted at that time. *See* Ex. 7 at 3-5.[11]

Eagle also cites to a May 2017 Office Action Response (Ex. 12) and accompanying Kannan Declaration (Ex. 11), but these documents similarly focus on changes in the amount of vasopressin and the total amount of specified and unspecified impurities over time as evidencing surprising and unexpected results that support the patentability of the claimed inventions. There is no special significance attributed to any particular vasopressin degradation products or, more pertinently, to the list of particular degradation products specified in Table 1 of the specification.

In sum, Eagle cannot point to any evidence of patentee lexicography or disavowal with respect to the term "vasopressin degradation products," let alone

[11] The limitation was added by a later amendment. *See* Ex. 12 at 2.

evidence sufficient to meet the "exacting standards" needed to overcome the presumption that the term carries its plain and ordinary meaning.[12] And, since there does not appear to be any confusion as to what that ordinary meaning is, the Court should adopt Par's proposal that the term carries its ordinary meaning, and that no further construction is required.

2. Eagle's Answering Position:

Par's uninformative "ordinary meaning" construction of the "vasopressin degradation products" term—which Par still has not clearly defined—ignores its own lexicography in favor of references to portions of the intrinsic evidence that have nothing to do with this term. And although Par contends that the term has a well-known ordinary meaning, it has provided no evidence. This is of particular importance here, where Par's proposed non-construction of a technical term ignores the express definition provided in the specification. *See 3M Innovative Props Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1374 (Fed. Cir. 2003) ("Because 3M expressly acted as its own lexicographer . . . the definition in the specification controls . . . regardless of any potential conflict with the term's ordinary meaning.").

[12] In addition to the cases cited above at pp. 3-4, *see also Cont'l Circuits LLC v. Intel Corp.*, 915 F.3d 788, 797 (Fed. Cir. 2019) ("To disavow claim scope, the specification must contain expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope.") (internal quotations omitted).

Specifically, the patent states that "[v]asopressin and associated degradation products or peptides ***are*** listed in TABLE 1." *E.g.*, Ex. 1 ('239 patent) at 3:1–3 (emphasis added). Table 1 then lists the sequence of vasopressin as SEQ ID No. 1, followed by identification of the sixteen "degradation products or peptides" as SEQ ID Nos. 2–17. *E.g.*, *id.* at 3:1–39. Notably, in defining "vasopressin" for purposes of the claims, Par insisted that the definition refer to "SEQ ID No. 1" from Table 1 of the patent, pointing to column 3 of the patent for support. *See* Ex. 24 (Par's February 20, 2019 Proposed Constructions and Intrinsic Evidence) at 1–3. Par has not explained why that same intrinsic evidence does not support specifying the SEQ ID Nos. from Table 1 in the definition of "vasopressin degradation products."

Contrary to Par's assertion, nowhere does the specification or prosecution history suggest that other "vasopressin degradation products" were known to, or contemplated by, the inventors. Instead, the definition ascribed by Table 1 is consistently used throughout the entire patent specification and prosecution history, thus further supporting Eagle's construction. *See, e.g.*, *Astrazeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1051–52 (Fed. Cir. 2010) ("When a patentee uses a claim term throughout the entire patent specification, in a manner consistent with only a single meaning, he has defined that term 'by implication.'"). For instance, Example 1 of the patent describes the protocol by which the vasopressin degradation products may be identified. *E.g.*, Ex. 1 ('239 patent) at 16:5–19:45. This method yielded

"vasopressin degradation products" identified in Table 1. *E.g.*, *id.* at 19:10–45 (Table 3); *see also* Ex. 25 (Amiji Decl.) ¶ 21. Likewise, during prosecution, the inventors submitted a declaration that measured vasopressin "degradation," which also identified only "vasopressin degradation products" from Table 1. Ex. 11 (Kannan Decl. (Appl. No. 14/717,877 ('239 patent)) (May 22, 2017)) ¶ 6; *see also* Ex. 8 (Vandse Decl. (Appl. No. 14/717,877 ('239 patent)) (Aug. 11, 2015)) ¶ 5.

To be sure, the patent identifies other "impurities" that might be found in a vasopressin formulation, but those would not be classed as "vasopressin degradation products." For example, an "AVP-Dimer" is not a product of degradation of a vasopressin molecule, but rather is a complex formed by the joining of two vasopressin molecules. Ex. 25 (Amiji Decl.) ¶ 22. Other "unidentified substances" could not be classified as "vasopressin degradation products" either. *Id.* ¶ 23. Notably, Par concedes that in adding the total amount of the sixteen identified "vasopressin degradation products," the "AVP-dimer" and the "unidentified substances" denominated "UI-____," the patent uses the term "Total *Impurities*." *E.g.*, Ex. 1 ('239 patent) at 19:45–57 (Example 2) (describing Fig. 9, which measures percent "Total Impurities"). If the patentees considered these compounds all to be included within the "vasopressin degradation products" term, they could have, and would have, used the term "Total *Vasopressin Degradation Products*." *See, e.g.*, *Sanofi-Aventis U.S. LLC v. Merck Sharp & Dohme Corp.*, 2018 WL 389183, at *5–

6 (D. Del. Jan. 12, 2018) ("The specifications do not appear to use the words 'thread' and 'spline' interchangeably. . . . There is no reason to conclude that the patents use the word 'spline' to refer to a type of 'thread.'").

Further, Par's insistence on conflating "vasopressin degradation products" and "impurities" renders the claims effectively impossible to practice. At the claimed pH, the "Total Impurities" for the claimed formulations, as shown in Figure 9, is almost ***20%***. *E.g.*, Ex. 1 ('239 patent) at 19:45–57 (Example 2) (citing Fig. 9); *see also* Ex. 25 (Amiji Decl.) ¶ 20. That figure is dramatically higher than the ***0-2%*** figure the claims require for the "vasopressin degradation products" at the same pH. Thus, if "vasopressin degradation products" and "impurities" refer to the same things—as Par appears to suggest—then the patent would not teach how to meet the ***0-2%*** limitation of the claims, as demonstrated by its own specification disclosing the impurity level at ***20%***. *AIA Eng'g. Ltd. v. Magotteaux Int'l S/A*, 657 F.3d 1264, 1276–79 (Fed. Cir. 2011) ("where . . . the specification reveals a special meaning for a term that differs from the meaning it might otherwise possess, that special meaning governs, particularly when it also serves to avoid an inoperable claim construction.") It is thus clear that the applicants did not intend to include all such impurities within the 2% "vasopressin degradation product" limitation.

Par also raises a claim differentiation argument that the independent claims must "encompass any vasopressin degradation products, not just particular ones" on

the basis that some of the dependent claims are limited to a subset of the degradation products listed in Table 1. But that argument is unavailing. The doctrine of claim differentiation "takes on relevance in the context of a claim construction that would render additional, or different, language in another independent claim superfluous." *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1381 (Fed. Cir. 2006). And importantly, "claim differentiation 'can not [sic] broaden claims beyond their correct scope.'" *See id.* Here, Eagle's construction does not render any claim limitations superfluous, as the dependent claims with limitations to a subset of the degradation products are clearly narrower than the independent claims without such limitations. Thus, Par's attempt to broaden the scope of the independent claims on the basis of claim differentiation is improper.

At base, the patentees specifically defined what should be considered "vasopressin degradation products," as opposed to "total impurities," in the specification by reference to Table 1. Par cannot now disavow that lexicography through its "ordinary meaning" construction. *See, e.g.*, *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) (a "claim term will not receive its ordinary meaning if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history").

3. Par's Reply Position:

As Par predicted, Eagle does not contend either that its proposed construction reflects the ordinary meaning of the term "vasopressin degradation products," or that the Table that it incorporates into its construction includes all possible vasopressin degradation products. Instead, Eagle argues that the patentees used their "own lexicography" and provided an "express definition" in the specification. *Supra* at 18-19. It is well-settled, however, that "[t]o act as its own lexicographer, a patentee must ***clearly set forth a definition*** of the disputed claim term other than its plain and ordinary meaning." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (emphasis added). "It is not enough for a patentee to simply disclose a single embodiment or use a word in the same manner in all embodiments, the patentee must ***'clearly express an intent' to redefine the term***." *Id*. (quoting *Helmsderfer v. Bobrick Washroom Equip., Inc.*, 527 F.3d 1379, 1381 (Fed. Cir. 2008)) (emphasis added). Indeed, the *3M* case cited by Eagle illustrates the type of clear language that the Federal Circuit requires in order to find that a patentee has acted as its own lexicographer. *See 3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1374 (Fed. Cir. 2003) (noting that the patent specification explicitly defined claim term by stating that "[e]mbossed ***means*** a topography on a web…") (emphasis added).

a. The Patentees Did Not Act as Their Own Lexicographer

Eagle cannot meet its heavy burden. It cites neither an express definition nor anything in the intrinsic evidence demonstrating a clear intent to redefine the term "vasopressin degradation products." Instead, Eagle focuses on Table 1 of the '239 patent which is described as listing "Vasopressin and associated degradation products or peptides . . ." Ex. 1 ('239 patent) at 3:1-3. Table 1 lists the name and sequence for vasopressin and sixteen different degradation products. *Id*. at 3:1-38. Nowhere does the patent "clearly assign a unique definition" to "vasopressin degradation products," distinguish this term from the prior art, disclaim any subject matter, or describe that only the degradation products listed in Table 1, and not others, are "important to the invention." *See CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1367 (Fed. Cir. 2002).

Eagle's argument is that the patentees provided an express definition, and thereby acted as their own lexicographer, when they stated in the specification that "[v]asopressin and associated degradation products are listed in Table 1 below." *See supra* at 19. Not so. There is no dispute that the compounds listed in Table 1 "are" vasopressin degradants, but there is no indication either that the patentees intended the list to be exhaustive of all possible "vasopressin degradation products," or that they intended to exclude from that term any degradation products not included within that list. Rather, the cited statement simply indicates that Table 1 contains

vasopressin degradation products; it is not an explicit statement that "vasopressin degradation products" refers ***only*** to the compounds listed in that table. Thus, Eagle cannot overcome the "heavy presumption" that "vasopressin degradation products" should be construed in any way except its plain and ordinary meaning. *CCS Fitness*, 288 F.3d at 1366.

Eagle argues that this is somehow inconsistent with the parties' agreement that the term "vasopressin" should be construed with reference to its Sequence ID No. identified in the specification. *See supra* at 19. There is no such inconsistency. As a threshold matter, a stipulation by the parties to narrow the disputed issues by agreeing to a stipulated construction of a particular term does not in any way indicate any agreement or disagreement with any other position as to a different term. Moreover, the circumstances are not analogous. The definition does not even refer to Table 1, and in any event, there are many passages throughout the specification that point to the agreed upon definition, including for example that the specification explicitly says "[v]asopressin is a nonapeptide, illustrated below (SEQ ID NO. 1)" (Ex. 1 ('239 patent) at 2:33-34) and that Table 3 recites "Vasopressin (Arginine Vasopressin, AVP)" and refers to "SEQ ID NO.: 1 (disulfide bridge between cys residues)" (*id.* at col. 19), as well as the additional information provided in the Sequence Listing at columns 25 and 26. Thus, the meaning of vasopressin as used in the '239 patent is clear from the specification. The reference in Table 1 to

"Vasopressin" and its "Sequence" simply confirms the meaning found throughout the rest of the specification.

Eagle argues that the supposed "definition ascribed by Table 1" is "consistently used through the entire patent specification and prosecution history." *See supra* at 19. Yet, they point to no other instance in which the patentees purported to say either that the degradation products listed in Table 1 were meant to be an all-encompassing list of all possible "vasopressin degradation products," or that that term was meant to exclude any degradation products not listed in the Table.

b. Vasopressin Dimer Is a Vasopressin Degradation Product Not Found in Table 1

Moreover, Figures 3 – 5 and Table 3 identify a vasopressin degradation product referred to as "Dimer-AVP" or "Dimeric-vasopressin" which is not included in Table 1. Ex. 1 ('239 patent) at Figs. 3-5, col. 19. *See also* Ex. 32 (Kirsch Decl.) ¶¶ 6-8.

Eagle dismisses the references to this vasopressin "dimer," arguing that a "dimer" is an impurity rather than a degradation product. *See supra* at 20. However, the specification explains that "[t]o analyze degradation products of vasopressin that can be present in an illustrative formulation of vasopressin, gradient HPLC was performed to separate vasopressin from related peptides and formulation components," and they then report in Table 3 those that were found at

a concentration of 0.10% or more. Ex. 1 ('239 patent) at 16:9-12; 18:56-58. In view of the other components (none of which are peptides), the "related peptides"—which would include vasopressin-dimer—can only result from the degradation of vasopressin.[13]

Furthermore, consider a hypothetical example in which one has an aqueous solution that contains 100 vasopressin molecules. The circumstances are such that after a day in storage, two vasopressin dimers are formed—*i.e.*, there are two instances in which a pair of vasopressin molecules have cross-linked with one another to form a vasopressin dimer. At that point, the vasopressin will have degraded and the solution would only have 96% of the vasopressin it originally had (because 4 of the original 100 vasopressin molecules have been chemically transformed into two dimers). Ex. 32 (Kirsch Decl.) ¶ 8.

[13] *See also* the declarations of Sunil Vandse and Vinayagam Kannan submitted during prosecution of the '239 patent. Exs. 8, 11. In those declarations, the inventors also referred to "vasopressin degradation products," "related peptides," "associated peptides," or other similar phrases, and referred to them collectively as impurities that can be present in an illustrative formulation of vasopressin. Moreover, the Vandse declaration specifically referred to the dimer—along with other related peptides explicitly referenced in Table 1, such as Gly-9 AVP, Glu-4 AVP, Asp-5 AVP, D-Asn AVP, and Acetyl AVP—as a related peptide impurity or identified related peptide. Ex. 8, ¶ 5. The inventors' choice to describe the dimer as they described other vasopressin degradation products listed in Table 1, confirms their intent to include that dimer as a vasopressin degradation product.

Accordingly, the dimer's inclusion in Table 3 and Example 1 demonstrates that Table 1 is not intended to be an all-encompassing, exclusive list of all possible vasopressin degradation products. [14]

c. Adopting Par's Construction Would Not Render the Claimed Inventions Inoperative

Eagle's final argument is that construing "vasopressin degradation product" in accordance with its ordinary meaning, and not restricted to just those degradants listed in Table 1, purportedly would "render[] the claims effectively impossible to practice," citing one figure from Example 2 (Figure 9) in which the "total impurities" are listed as being higher than 20%. *Supra* at 21. That argument, however, rests on faulty premises, including at a minimum that the quoted 20% impurity figure reflects impurities resulting from the pharmaceutical compositions and conditions claimed by the inventors.

Example 2 relates to an accelerated degradation study, wherein "vasopressin formulations were prepared in 10 mM citrate buffer diluted in isotonic saline across a range of pH" and incubated "at 60 ºC for one week." Ex. 1, 19:49-54. A

[14] Eagle disputes Par's and its expert's characterization of vasopressin "dimer" as a vasopressin degradation product. While Par believes it and its expert are correct, the dispute ultimately is one for another day, as it involves the application of the definition to a particular compound that may or may not be relevant to issues of infringement and/or validity at some point in the future. The Court need not resolve the dispute to conclude that the patentees did not intend Table 1 to be an all-encompassing or exclusive list of "vasopressin degradation products."

POSA would understand that this diluted sample does not reflect the pharmaceutical compositions claimed in the '239 patent for a variety of reasons, including that the claimed formulation must contain "acetic acid, acetate or a combination thereof," while the composition tested included a citrate buffer instead, and that the experimental conditions (diluting the composition in saline solution and then incubating it at 60 ºC for one week) are not reflective of the conditions in which they are likely to be stored.[15] Testing the stability of a different composition under different, accelerated storage conditions does not in any way suggest that the claimed inventions are somehow "effectively impossible to practice," as Eagle asserts.

4. Eagle's Sur-Reply Position:

Par's attempt to overcome its lexicography fails. The '239 patent states explicitly that "[v]asopressin and associated degradation products…***are*** listed in TABLE 1" Ex. 1 at 3:1–3. It thus provides notice of the compounds included in the 0-2% claim limitation. Par does not dispute the patent never refers to any other compound as a "vasopressin degradation product." Other byproducts, such as vasopressin dimer, are classed as "impurities." *Id.* at 16:3–19:57.

Par relies heavily on its assertion that the patent identifies vasopressin dimer

[15] 60 ºC equates to 140ºF—*i.e.* roughly twice room temperature.

as a "degradation product," when it is not listed in Table 1. Not so. The dimer is consistently labeled as an "impurity." Par's only support is the extrinsic declaration of Dr. Kirsch, which cannot overcome the intrinsic record. In any event, Dr. Kirsch's opinions are internally inconsistent. He states "vasopressin degradation products" arise "when the covalent bonds between various atoms within vasopressin are broken or transformed." Ex. 32 (Kirsch Decl.) ¶ 5. Yet he acknowledges that dimer formation involves association of two vasopressin molecules. *Id.*, ¶ 6. The two complexed vasopressin molecules are not degraded. Ex. 44 (Suppl. Amiji) ¶ 4.

Par's other arguments fare no better. Contrary to Par's assertion, lexicography need not follow any particular form, and need not distinguish a term from the prior art, disclaim subject matter, or state a term is "important to the invention," all of which are ***alternative*** bases for "constrict[ing] the ordinary meaning of a claim term." Par Reply at 24; *CCS Fitness*, 288 F.3d at 1359. Here, the specification states "vasopressin degradation products" of the invention "***are*** listed in TABLE 1," thereby assigning a "unique definition" to a term that has no established ordinary meaning. Indeed, Dr. Kirsch does not explain how a POSA would determine if an impurity "result[s] from chemical degradation of vasopressin" (Ex. 32 ¶ 5) as opposed to some other mechanism.

Notably, Par concedes "[t]he reference in Table 1 to 'Vasopressin' and its 'Sequence' simply confirms the meaning found throughout the rest of the

specification." Par Reply at 25–26. The same is true of Table 1's list of "vasopressin degradation products." Par's assertion that there is "no other instance" where the patent defines the term with respect to Table 1 (*id.* at 26) is incorrect. The specification states, in a section titled "Vasopressin ***and Peptides of the Invention***," that the vasopressin degradation products are "***detailed in EXAMPLE 1 and TABLE 1 below***." Ex. 1 at 2:3–44.

Par's hypothetical equating loss of vasopressin from solution with degradation is flawed. Par Reply at 27. Of course, vasopressin can be lost from a solution due to processes other than degradation. The complexing of vasopressin molecules to form dimers results in loss of vasopressin monomers, but not from degradation. Ex. 44 (Suppl. Amiji) ¶¶ 4–5.

Par attempts to explain away the "Total Impurities" percentage in Example 2 based on the temperature and formulation used. Par Reply at 28–29. But the '239 patent claims are not limited to any particular temperature, and Par identifies no evidence that use of citrate buffer, rather than "acetic acid, acetate or a combination thereof," makes any material difference; they are described as interchangeable. Ex. 1 at 11:45–53.

Finally, Par's argument that this term can encompass any number of unspecified compounds would render the claims indefinite. This is clear from the fact the parties' experts cannot even agree whether a vasopressin dimer qualifies.

At base, the patentees clearly defined "vasopressin degradation products" by reference to Table 1, and should be held to that lexicography here.

B. "ACETATE BUFFER"

1. Par's Opening Position:

The disputed term "acetate buffer" appears in each of the independent claims of the '223 and '478 patents. The parties' respective proposed constructions are as follows:

Par's Proposed Constructions	Eagle's Proposed Constructions
Ordinary meaning, no construction necessary	"A solution containing a mixture of acetic acid and acetate that is capable of resisting changes in pH upon the addition of acidic or basic substances (acetic acid for pH adjustment is not an acetate buffer)."[16]

Buffers may be added to pharmaceutical formulations to help maintain a desired pH. The first part of Eagle's proposed construction (*i.e.*, up to the point of the parenthetical) appears to be an attempt to construe the ordinary meaning of the

[16] '478 claim 1 specifically recites "10mM acetate buffer." "mM" is short-hand for millimolar, which is a unit of measure of the concentration of a substance in solution. Eagle's proposed construction for the term "10 mM acetate buffer" is the same as for "acetate buffer" except it adds the following italicized clause: "A solution containing a mixture of acetic acid and acetate, *with a total concentration of 10 mM*, that is capable of resisting changes in pH . . ." That aspect of Eagle's construction is consistent with the ordinary meaning of the term, and is not in dispute between the parties.

term "acetate buffer." Although Par would quibble with the particular wording chosen,[17] there is no dispute that, as a general matter, a buffer requires the presence (in solution) of an acid and its conjugate base, or that a buffer resists changes in pH when small amounts of acid or base are added to the solution. *See, e.g.*, Ex. 13 (Mohan) at 8 ("Buffers are aqueous systems that resist changes in pH when small amounts of acid or base are added. Buffer solutions are composed of a weak acid (the proton donor) and its conjugate base (the proton acceptor).").[18]

Thus, the parties' dispute is not really about the ordinary meaning of the word "buffer." It is instead a dispute about the propriety of Eagle's insertion, by way of a parenthetical, of a proposed negative limitation that would exclude particular substances from the scope of the limitation—*i.e.*, whether the Court should declare as a matter of claim construction that "acetic acid for pH adjustment" is *not* an "acetate buffer."

As a threshold matter, it is not even clear what Eagle seeks to exclude by way of its parenthetical—are they suggesting that acetic acid, by itself and in the absence

[17] For example, it is redundant to refer to a solution containing "a mixture" of two components, because a solution containing those components would necessarily include "a mixture" of them.

[18] Ex. 13 (Mohan) is art cited to the examiner during prosecution of the '223 patent and was identified by Eagle in the parties' Joint Claim Construction Statement as supporting its proposed construction.

of other components, is not a buffer, or that if it is included in a formulation for one purpose ("for pH adjustment") it is not a buffer, but if it is included for a different purpose it might be? Eagle's proposed construction would itself have to be construed to understand what it means.

Equally, if not more importantly, Eagle's proposed negative limitation by way of the parenthetical is not a proper construction of the meaning of the words "acetate buffer," but is instead an attempt by Eagle to raise an infringement issue under the guise of claim construction. That is improper.

As the Federal Circuit explained in *Am. Piledriving Equip., Inc. v. Geoquip, Inc.*, 637 F.3d 1324, 1331-32 (Fed. Cir. 2011), "[i]t is well settled that the role of a district court in construing claims is not to redefine claim recitations or to read limitations into the claims to obviate factual questions of infringement and validity"; it is instead "to give meaning to the limitations actually contained in the claims." Being mindful of this principle is "particularly important" where "the alleged infringer is attempting to import a limitation to exclude specific features of the accused product." *Proprietect L.P. v. Johnson Controls, Inc.*, No. 12-12953, 2013 WL 6795238, at *7 (E.D. Mich. Dec. 23, 2013) (rejecting argument that construction

of "the surface" be "further limited to *exclude* 'an epoxy gasket with tape vents'") (emphasis in original).[19]

Here, as noted above, the first part of Eagle's proposed construction is at least an attempt to construe the meaning of the actual words of the claim. But, Eagle's proposed construction does not stop there—

[redacted]

[19] *See also, e.g., Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1331 (Fed. Cir. 2006) (courts are forbidden from "tailoring a claim construction . . . to reach a preconceived judgment of infringement or noninfringement," that is, "from biasing the claim construction process to exclude or include specific features of the accused product or process"); *Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1367 (Fed. Cir. 2008) ("[a]lthough 'it is appropriate for a court to consider the accused device when determining what aspect of the claim should be construed,' it is not appropriate for the court to construe a claim solely to exclude the accused device.") (citation omitted).

[redacted]

The relevant fact here is that there is no support for Eagle's proposed negative limitation anywhere in the intrinsic evidence it cites. *See, e.g., Intellectual Ventures I, LLC v. Motorola Mobility, LLC*, 13 F. Supp. 3d 369, 400 (D. Del. 2014) ("A negative limitation will not be imparted to the claim term absent support in the specification or prosecution history") (citing *Omega Eng'g Inc. v. Raytek Corp.*, 334 F.3d 1314, 1322–23 (Fed. Cir. 2003)); *Linear Tech. Corp. v. Int'l Trade Comm'n*, 566 F.3d 1049, 1060 (Fed. Cir. 2009) ("Thus, because there is no basis in the patent specification for adding the negative limitation—excluding monitoring voltage—we hold that the Commission erred in construing this limitation.").

Throughout the specifications of the '223 and '478 patents, for example, the term is used in accordance with its ordinary, well-understood meaning in the art. The '223 patent provides, for instance:

> Effect of Buffer and Divalent Metals on Vasopressin Formulation.
>
> To determine whether different combinations of buffers and use of divalent metals affect vasopressin stability, vasopressin formulations with varying concentrations of citrate and acetate buffers and variable concentrations of calcium, magnesium, and zinc ions were prepared. Solutions of 0 mM, 10 mM, 20 mM, and 80 mM calcium, magnesium,

> and zinc were prepared and each was combined with 1 mM or 10 mM of citrate or acetate buffers to test vasopressin stability.

'223 patent (Ex. 6) at 61:7-17; *see also id.* at 50:57-65, Example 12 (col. 102), Table 48 (cols. 103-104), Table 51 (col. 104), Table 56 (cols. 107-108), 128:11-14; '478 patent (Ex. 2) at 11:21-29, 19:58-67, 20:49-51. Nowhere does the patent specification state that "acetic acid for pH adjustment" is not an acetate buffer. Likewise, nothing in any of the statements cited by Eagle from the prosecution histories of any of the patents-in-suit or other patents reflect any intent by the patentees to deviate from the ordinary meaning of that term. *See Cont'l Circuits*, 915 F.3d at 797 (Fed. Cir. 2019) ("To disavow claim scope, the specification must contain expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope.") (internal quotations omitted).

Accordingly, the Court should construe the term "acetate buffer" as having its plain and ordinary meaning, and reject Eagle's attempt to interject an improper negative limitation as an add-on to that ordinary meaning.

2. Eagle's Answering Position:

The '223 and '478 patents both require administering a vasopressin formulation having a particular pH, which comprises, *inter alia*, an "acetate buffer" to maintain that pH. *See* Ex. 6 ('223 patent) claim 1; Ex. 2 ('478 patent) claim 1. As an initial matter, Par contends that the "acetate buffer" term should be given its "ordinary meaning," but other than "quibbling," it does not dispute that the portion

of Eagle's construction before the parenthetical accurately reflects that ordinary meaning. The Court therefore should at least adopt that undisputed portion in its construction.

The Court also should adopt Eagle's parenthetical or at least adopt that limitation in its claim construction ruling, because it is mandated by prosecution history disclaimer. In that regard, Par's Opening Brief makes clear that it intends to argue that using acetic acid for pH adjustment can somehow be captured within the scope of the term "acetate buffer" in the asserted claims. But as explained below, that is directly contrary to positions it took during prosecution to secure claims in related patents. Contrary to Par's assertion, giving effect to its prosecution disclaimer is not an infringement question but one of claim construction as a matter of law. *See, e.g.*, *Chimie v. PPG Indus., Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005) ("use of the prosecution history ensures that claims are not construed one way in order to obtain their allowance and in a different way against accused infringers" (citation omitted)). Courts in this District routinely make clear the negative impact of prosecution disclaimer on the construction of claim terms, including through use of parentheticals just as Eagle has proposed here. *See, e.g.*, *Transcend Medical, Inc. v. Glaukos Corp.*, C.A. No. 12–830, 2015 WL 263612, at *8, *12 (D. Del. Jan. 16, 2015) (construing disputed terms to include defendant's proposed negative

limitations where the patentee made statements during prosecution that the disputed terms did not include the negative limitation).

It is axiomatic that "[p]rosecution disclaimer can arise from both claim amendments and arguments made to the PTO." *See Tech. Props. Ltd., v. Huawei Techs. Co.,* 849 F.3d 1349, 1357–58 (Fed. Cir. 2017). Thus, where a patentee "insist[s] that its invention differed from the prior art" during prosecution, that amounts to "a deliberate surrender of claim scope." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1327 (Fed. Cir. 2003). Disclaimer in an application will apply equally to related applications, including continuations-in-part. *See, e.g.*, *Teva Pharm. USA, Inc. v. Sandoz, Inc*., 789 F.3d 1335, 1343 n.5 (Fed. Cir. 2015) ("we have said before, and reaffirm today, that past and future prosecution of related patents may be relevant to the construction of a given claim term") *Capital Mach. Co. v. Miller Veneers, Inc*., 524 F. App'x 644, 649 n.1 (Fed. Cir. 2013) ("Disclaimer during the prosecution of one patent applies to other patents in the same family when the patents are directly related, such as through a parent-child relationship."). Par did just that here.

U.S. Patent No. 9,981,006 claims priority through the asserted '209, '526 and '239 patents to U.S. App. No. 14/610,499. Ex. 26 ('006 patent). That is the same application to which the '223 and '478 patents claim priority. *See* Ex. 6 ('223 patent); Ex. 2 ('478 patent). The '006 patent is therefore related to the '223 and '478

patents. And because the term to be construed (acetate buffer) is identical to the term that was at issue during prosecution of the '006 patent, the prosecution history of the '006 patent is particularly relevant in construing that same term. *Z4 Techs., Inc. v. Microsoft Corp*., 507 F.3d 1340, 1348 (Fed. Cir. 2007) ("We presume, unless otherwise compelled, that the same claim term in the same patent or related patents carries the same construed meaning."); *Capital Mach*, 524 F. App'x at 649.

During prosecution of the '006 patent, the examiner rejected all pending claims under both anticipation and obviousness based on a 2015 label for Par's Vasostrict® product. Ex. 15 (Response to Non-Final Office Action (Appl. No. 15/688,305 ('006 patent)) (Jan. 26, 2018)) at 6–7(noting that pending claims 16–33 were rejected as anticipated and obvious in view of the 2015 Vasostrict® Label). That prior art label disclosed that the pH of the vasopressin formulation was "***adjusted with acetic acid***." Ex. 27 (2015 Vasostrict® Label § 11). In response, Par amended each claim "to recite that the unit dosage form contains about 1 mM to about 10 mM ***acetate buffer***." Ex. 15 (Response to Non-Final Office Action (Appl. No. 15/688,305 ('006 patent)) (Jan. 26, 2018)) at 7. Par then argued that the 2015 Vasostrict® label "***does not disclose use of about 1 mM to about 10 mM acetate buffer*** in a formulation," and therefore "does not teach each and every element." *See id*. The examiner withdrew the rejection and the '006 patent issued.

Notably, in overcoming the examiner's rejection, Par relied on the amendment adding "1 mM to about 10 mM ***acetate buffer***" for ***both*** anticipation and obviousness. That is, Par took the position that not only is adjusting the pH with acetic acid ***different*** from using an acetate buffer (for anticipation), but further that a POSA would not have found the use of "acetate buffer" obvious based on the prior art teaching the use of acetic acid for pH adjustment (for obviousness). Ex. 15 (Response to Non-Final Office Action (Appl. No. 15/688,305 ('006 patent)) (Jan. 26, 2018)) at 6–7; *see also* Ex. 25 (Amiji Decl.) ¶ 27. That latter position, in particular, is directly opposite to the position that Par has taken here, *i.e.*, that the "acetate buffer" term's "ordinary, well understood meaning in the art" ***includes*** using acetic acid for pH adjustment.[20] Par should not be permitted to take opposite positions on the state of the art to serve its interests based on differing circumstances. At a minimum, the fact that Par itself has had conflicting views of the state of the art

[20] Notably, Par made the same distinction before the FDA, as it did before the Patent Office. Ex. 25 (Amiji Decl.) ¶ 28. As Dr. Amiji explains in his declaration, in 2016, Par sought to modify its 2015 Vasostrict® formulation, which was also the prior art at issue during prosecution of the '006 patent. *Id*. In seeking to modify its 2015 Vasostrict® formulation, Par explained to the FDA that whereas the 2015 formulation contained acetic acid for pH adjustment, its new 2016 formulation added "sodium acetate ***for buffering***." *Id*. Par then revised its 2015 Vasostrict® Label to reflect this change by removing the phrase "***adjusted with acetic acid*** to pH 3.4–3.6" and replacing it with "sodium ***acetate buffer*** adjusted to a pH of 3.8." *Id*.

suggests that Par's "ordinary meaning" constructions cannot meaningfully define the scope of the claims at issue.

Indeed, by not only distinguishing, but also advocating that a formulation that uses an "acetate buffer" is ***nonobvious*** over another that uses "acetic acid" for pH adjustment, Par disclaimed inclusion of acetic acid for pH adjustment within the "acetate buffer" term. *See Huawei*, 849 F.3d at 1357–58; *see also Kraft Foods Grp. Brands LLC v. TC Heartland*, LLC, C.A. No. 14-028-LPS, 2016 WL 873435, at *9 (D. Del. Mar. 7, 2016) (patentee's narrowing amendment in response to the examiner's rejection amounted to disclaimer). That disclaimer applies equally to the related '223 and '478 patents. *See, e.g.*, *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1343 (Fed. Cir. 2015) ("A statement made during prosecution of related patents may be properly considered in construing a term common to those patents, regardless of whether the statement pre- or post-dates the issuance of the particular patent at issue."). In fact, disclaimer applies with heightened force here because the term to be construed—acetate buffer—is the very term that Par defined during the prosecution of the related, '006 patent, and Par's amendment adding that term was ***dispositive*** to the patent's issuance. *See, e.g.*, *Z4 Techs., Inc. v. Microsoft Corp.*, 507 F.3d at 1348 ("We presume, unless otherwise compelled, that the same claim term in the same patent or related patents carries the same construed meaning."); *Capital Mach*, 524 F. App'x at 649 ("we have held that the prosecution history regarding a

claim term is pertinent when interpreting the same term in both later-issued and earlier-issued patents in the same family.")

The specifications the '223 and '478 patents too confirm the distinction between using "acetic acid" for pH adjustment from that of "acetate buffer" in vasopressin formulations. Both specifications provide that "[n]on-limiting examples of *buffers* include . . . *acetate*." Ex. 2 ('478 patent) at 11:21–29; *see also* Ex. 6 ('223 patent) at 50:57–65 (same). "Acetic acid" is absent from the list of buffers. In contrast, "acetic acid" is described as an "excipient." *See* Ex. 2 ('478 patent) at 11:59–12:3 ("Further excipients that can be used in a composition of the invention include . . . acetic acid"); *see also* Ex. 6 ('223 patent) at 51:29–41 (same). Had Par intended that "acetic acid" could be considered a "buffer," it would have listed it in the list of exemplary buffers in the specification. *See, e.g.*, *Sanofi-Aventis*, 2018 WL 389183, at *5–6 (refusing to construe "thread" as including "spline," because the terms are not used "interchangeably. . . . Rather, the patents differentiate between the two."); *see also* Ex. 25 (Amiji Decl.) ¶ 29.

Notably, Par concedes that a negative limitation may be appropriate in a claim construction where there is "support in the specification or prosecution history." *See, e.g.*, *Intellectual Ventures I, LLC v. Motorola Mobility, LLC*, 13 F. Supp. 3d 369, 400 . That is the case here, as both the specification and the prosecution history make clear that acetic acid for pH adjustment is not included within the term "acetate

buffer." The Court therefore should make this clear in its construction, or at least its claim construction ruling. *See, e.g., SkinMedica, Inc. v. Histogen Inc.*, No. 09–CV–122 JLS (NLS), 2011 WL 2066619, at *6–*8 (S.D. Cal. May 24, 2011) (construing disputed terms to exclude, by parenthetical, limitations the patentee excluded by acting as its own lexicographer), *aff'd*, 727 F.3d 1187 (Fed. Cir. 2013).

3. Par's Reply Position:

As Eagle's brief confirms, the principal dispute between the parties is whether the Court should adopt the negative parenthetical in Eagle's proposed construction as a matter of "prosecution history disclaimer." *See supra* at 38-43. The Court can and should resolve that dispute by rejecting Eagle's disclaimer arguments and proposed parenthetical.

a. Ordinary Meaning

Par does not believe that the Court need provide an express construction of the ordinary meaning of the term "acetate buffer" to resolve the parties' dispute. *See, e.g., ActiveVideo*, 694 F.3d at 1326 ("[t]he district court did not err in concluding that these terms have plain meanings that do not require additional construction"). To the extent the Court opts to provide an express construction, however, Par proposes that the Court model its construction on the language provided in the Mohan reference, which was cited during prosecution of the patents-in-suit and which Eagle cited as intrinsic evidence supporting its construction in the parties'

Joint Claim Construction Chart, rather than the language of Eagle's proposal which is untethered to any intrinsic or extrinsic evidence in the record.

As noted above, the Mohan reference cited by Eagle in the Joint Claim Construction Chart states in relevant part that "[b]uffers are aqueous systems that resist changes in pH when small amounts of acid or base are added. Buffer solutions are composed of a weak acid (the proton donor) and its conjugate base (the proton acceptor)." Ex. 13 (Mohan) at 8. Par contends that this wording is preferable to Eagle's unsupported wording because, as noted above, the words "a mixture of" in Eagle's construction are entirely unnecessary. Moreover, removing those words would avoid possible confusion by making clear that the solution need only contain the acid and its conjugate base in solution, not that the two must be separately added to the solution in order to form the buffer.[21]

[21] A POSA would understand, by way of example, that an acetate buffer can be formed by adding either acetic acid (the weak acid) or acetate (its conjugate base) without the other to an aqueous solution, or by adding them both to the solution. Ex. 32 (Kirsch Decl.), ¶ 12. This occurs because, for instance, when acetic acid is added to an aqueous solution, some proportion of the acetic acid will react with the water and deprotonate (i.e., lose a positively charged hydrogen ion (H^+)). *Id.* The chemical formula for acetic acid is CH_3COOH, such that when it deprotonates, it becomes CH_3COO^-, which is acetate. *Id.* Thus, when acetic acid is added to an aqueous solution, acetate will be formed in the solution, as a result of acetic acid's interaction with water molecules. *Id.* Moreover, the ability of a weak acid and its conjugate base to function as an effective buffer by resisting a pH change in solution depends on the initial pH value of the solution, total concentration of the buffer components, and their shared dissociation constant, such that the combination of

Accordingly, while Par continues to believe that the Court need not construe the term "acetate buffer" beyond giving it its plain and ordinary meaning, if the Court were to adopt an express construction, it should construe the term consistent with Mohan to mean "an aqueous solution that contains acetic acid and acetate and resists changes in pH upon the addition of small amounts of acid or base."

b. There Is No Prosecution Disclaimer

As explained in Par's opening brief, Eagle's proposed construction is, in reality, a not-so-thinly-veiled attempt by Eagle to have the Court engage in an infringement analysis under the guise of claim construction. Eagle does not dispute that it would be improper for the Court to conflate infringement with claim construction, but argues that its negative limitation can be justified on the grounds of prosecution history disclaimer arising out of the prosecution of a patent not in suit: U.S. Patent No. 9,981,006 (the '006 patent). *See supra* at 39-43. Eagle is wrong.

"The party seeking to invoke prosecution history disclaimer bears the burden of proving the existence of a clear and unmistakable disclaimer that would have been evident to one skilled in the art." *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1063-64 (Fed. Cir. 2016) (internal quotations omitted). "Where the alleged disavowal is

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acetic acid and acetate will act as a buffer in some solutions, but not others. *Id.*, ¶¶ 10-11.

ambiguous, or even amenable to multiple reasonable interpretations, [the Federal Circuit] has declined to find prosecution disclaimer." *Avid Tech., Inc. v. Harmonic, Inc.*, 812 F.3d 1040, 1045 (Fed. Cir. 2016) (citing *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1359 (Fed. Cir. 2003)); *see also Elbex Video, Ltd. v. Sensormatic Elecs. Corp.*, 508 F.3d 1366, 1371 (Fed. Cir. 2007) ("This doctrine does not apply 'where the alleged disavowal is ambiguous;' the disavowal must 'be both clear and unmistakable' to one of ordinary skill in the art.") (quoting *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1326 (Fed. Cir. 2003)).

Eagle cannot meet that heavy burden, because nowhere in the prosecution history cited by Eagle did the patentees ever state that acetic acid added to a formulation "for pH adjustment" cannot be an "acetate buffer," let alone do so in a clear and unequivocal matter.

In the cited prosecution history, the patentees amended the then-pending claims of the application that eventually issued as the '006 patent to recite that the claimed composition contains from "***about 1 mM to about 10 mM*** acetate buffer." Ex. 15 at 2 (emphasis added). Thus, the claims at issue did not recite acetate buffer alone; rather, they required the use of a specified concentration ("from about 1 mM to about 10 mM") of an acetate buffer. The patentees asserted that the claims, as amended, were patentable over the three prior art references cited by the examiner in rejecting their earlier claims—*i.e.*, the references identified as the "Label" (which

Eagle refers to as the "2015 Vasostrict® Label"), "Tidmarsh," and "Moberg." In particular, they argued that none of those references "disclose use of about 1 mM to about 10 mM acetate buffer in a formulation described herein." *Id.* at 6. Importantly, they did ***not*** say anything—one way or the other—about whether any of those references disclosed the use of an "acetate buffer."

Eagle argues that the patentees unequivocally disclaimed "acetic acid" added to a formulation "for pH adjustment" as an "acetate buffer" because the Label recited a vasopressin formulation that was "adjusted with acetic acid to pH 3.4 – 3.6." Ex. 27 at § 11. The patentees did no such thing. Eagle does not identify anywhere in the Label where it purportedly disclosed how much acetic acid was added. Thus, the patentees' statement merely reflects that, as is indisputably true, the disclosure in the Label of an unspecified amount of acetic acid does not disclose the use of "from about 1 mM to about 10 mM" of an acetate buffer.[22] That statement is not "a clear and unmistakable disclaimer" that "acetic acid for pH adjustment" can never

[22] Indeed, that is the very language that the patentees added to the claim in order to further distinguish it over the art. Moreover, as Dr. Kirsch explains, the mere presence of an acid and its conjugate base in a solution does not necessarily mean that they are acting as a buffer, as an acid and its conjugate base can serve to resist changes in pH in some aqueous solutions but not others, depending upon the particulars of the aqueous solution in which they are present. Ex. 32 (Kirsch Decl.), ¶ 10. Whether the presence of an acid and its conjugate base act as a buffer in a particular solution will depend on the pH of the solution and the concentration of the acid and the conjugate base in the solution. *Id.*

act as an acetate buffer in a vasopressin composition, as Eagle is required to show in order to justify its proposed negative limitation on the basis of prosecution history disclaimer. *Trivascular*, 812 F.3d at 1064; *Inline Plastics Corp. v. EasyPak, LLC*, 799 F.3d 1364, 1369 (Fed. Cir. 2015) (rejecting proposed limitation based on prosecution disclaimer when the proposed limitation "was not the basis of [inventor's] distinction"); *Avid Tech.*, 812 F.3d at 1046-47 (finding no clear and unmistakable disclaimer where the lower court read "more into the passage than is clearly there" and where "the language can easily be read to be distinguishing [the reference]" on different grounds).[23]

Accordingly, Eagle's assertion that "the term to be construed—acetate buffer—is the very term that Par defined during the prosecution of the related, '006 patent…" is simply not true. *See supra* at 42. The term that Eagle has asked the Court to construe in this case is "acetate buffer," which is not the same as "from about 1mM to about 10mM acetate buffer." The latter includes an important qualifier related to the concentration of the acetate buffer, which served to narrow the claims of the '006 patent and distinguish them over the prior art. Any alleged disclaimer is limited to the actual claim term at issue and the scope of what was

[23] As noted in Par's opening brief, it is not even clear what Eagle seeks to exclude—they do not specify any particular amount of acetic acid that is excluded, nor do they explain whether they are saying that when acetic acid is added to adjust pH it is not an acetate buffer, but that if it is added for some other purpose, it might be.

actually disclaimed. *See Plantronics, Inc. v. Aliph, Inc.*, 724 F.3d 1343, 1350 (Fed. Cir. 2013) ("[W]hen the patentee unequivocally and unambiguously disavows a certain meaning to obtain a patent, the doctrine of prosecution history disclaimer narrows the meaning of the claim ***consistent with the scope of the claim surrendered***.") (emphasis added).[24] Eagle cites no prosecution statements purportedly stating that acetic acid added to a composition "for pH adjustment" cannot act as an acetate buffer.[25]

[24] Eagle's argument that Par drew a distinction between pH adjustment and buffering before the FDA (*see supra* at 41 n.20) is similarly misguided. As a threshold matter, statements made outside of patent prosecution cannot form the basis for prosecution history disclaimer, so any such statements to the FDA have no relevance here. In any event, nothing Par said supports any alleged disclaimer of claim scope. Par simply pointed out to the FDA differences between its original, already-approved Vasostrict formulation and a reformulated Vasostrict formulation for which it was seeking FDA approval—one included acetic acid in an amount needed to adjust the formulation to a particular pH (3.4 – 3.6), while the other added sodium acetate in an amount sufficient for it to act as a buffer that maintained the formulation at a different pH (3.8). *See* Ex 30. The two formulations were using different components and they had different pHs, and pointing out those differences to the FDA when seeking approval for a revised formulation does not in any way support Eagle's assertion that the patentees disclaimed claim scope when prosecuting the '006 patent. As in the prosecution history discussed above, Par never said to the FDA that "acetic acid for pH adjustment" cannot serve as an acetate buffer.

[25] Eagle's assertion that acetic acid is listed in the specification as an "excipient," and not a "buffer" (*see* supra at 43) is both confusing and unavailing. It is undisputed that acetic acid is a component of an acetate buffer, so Par does not understand what point Eagle is making. In any event, Eagle does not attempt to argue that that statement could possibly constitute a clear and unmistakable disclaimer of claim scope.

Eagle emphasizes that the statements at issue were made in the context of obviousness (*supra* at 42), as if prosecution history disclaimer applies differently or more broadly in the context of obviousness than in other contexts. They cite no support, however, for such a proposition. In any event, however, it does nothing to change the analysis. The patentees argued that in order to establish even just a *prima facie* case of obviousness, "the prior art must disclose ***all elements and limitations of the claims***," and provide a motivation to combine the art with a reasonable expectation of success. Ex.15 at 6 (emphasis added). They then argued that the prior art cited by the examiner failed to meet that minimum threshold because, as discussed above, none of the three cited references, either alone or in combination, "disclose use of about 1 mM to about 10 mM acetate buffer in a formulation described [in the claims at issue]," and thus failed even collectively to disclose ***all*** elements of the claim. For the reasons expressed above, that truthful statement does not support Eagle's prosecution history disclaimer argument.

4. Eagle's Sur-Reply Position:

Par does not dispute its prosecution statements for the related '006 patent are binding. Par also does not dispute it overcame a rejection over its own Vasostrict® Label reciting use of acetic acid for pH adjustment by amending its claims to recite use of "acetate buffer." Par argues, however, that it should not be held to its disclaimer because its amended claim recited specific concentrations. Par Reply at

47–50. But the concentration was not material to Par's distinction, nor the Examiner's acceptance.

Prior to Par's amendment, the claim simply required inclusion of "acetate." Ex. 45 (Preliminary Amendment (Appl. 15/688,305) (Aug. 28, 2017)) at 2. The Examiner pointed out, however, that "[t]he Vasostrict® Label states that [the] vasopressin formulation also contains ***acetic acid*** to pH 3.4-3.6 (§ 11).…***[A]cetic acid dissociates in water to acetate…Therefore, the formulation comprises acetate***." Ex. 46 (Non-Final Rejection (Appl. 15/688,305) (Oct. 27, 2017)) at 9. In response, Par amended the claims to recite "about 1mM to about 10mM ***acetate buffer***." Ex. 15 (Response (Appl. 15/688,305) (Jan. 26, 2018)) at 6–7. Nowhere did the applicants suggest that the "acetic acid dissociate[d] in water to acetate" would generate an "acetate buffer"; the relevant distinction was the specific ***concentration*** of such buffer. And, even if the concentration provided an ***additional*** distinction—which Par never argued in prosecution—that "does not immunize" the "acetate buffer" distinction "from being used to construe the claim language." *Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1374 (Fed. Cir. 2007).

Further confirming that concentration alone was not the distinguishing feature, [redacted]

[26] Vasostrict® was originally known as "Pitressin" in FDA filings. Ex. 48.

[redacted] Using the molar mass of acetic acid (Ex. 44 (Suppl. Amiji) ¶¶ 9–10), there are approximately 3.7 x 10^{-6} moles of acetic acid per milliliter. [redacted]

The Court also should reject Par's transparent attempt to re-admit acetic acid through the back door based on its new "plain and ordinary meaning" construction asserted for the first time in Reply. The only apparent material difference between the parties' constructions is Par's omission of "a mixture of." Par Reply at 45. Its reasoning is apparent. It wants to argue that ***any*** composition with acetic acid and acetate is a "buffer," such that acetic acid alone would be covered because it dissociates in water to yield acetate.

Not only does Par's construction contradict its prosecution statements, it also misrepresents the teachings of Mohan. Mohan explicitly describes preparation of acetate buffer by ***separately*** adding acetic acid (weak acid) and sodium acetate (conjugate base), not by adding acetic acid alone. Ex. 13 at 19. As Dr. Amiji

explains, to have a buffering function, there must be a common ion effect. Ex. 44 ¶¶ 7–8. A weak acid (such as acetic acid), by itself, does not provide such a buffering effect. *Id.*

Although Dr. Kirsch asserts here that an "acetate buffer" ***could*** be formed by adding acetic acid alone (Ex. 32 ¶ 12), he stated exactly the opposite in a prior case involving the same term. Specifically, in *AstraZeneca Pharm. v. Teva Pharm. USA, Inc.*, No. 14-1478-GMS (D. Del.), the plaintiffs argued that an "acetate buffer" could be any "system comprising acetate that is capable of maintaining an approximately constant pH." Ex. 49 (*AstraZeneca* Decl.) ¶ 4. Dr. Kirsch disagreed, stating "[a] POSA would understand that ***a weak acid or its conjugate base*** provides ***minimal buffering*** at pH values far from the relevant pKa, so ***would not consider a solution to be an 'acetate buffer' merely because it contains some minimal concentration of acetate***." *Id.* ¶ 65; *see also id.* ¶ 8. According to Dr. Kirsch, to form an "acetate buffer" according to its "plain and ordinary meaning" would require "***both*** acetic acid ***and*** a conjugate base such as sodium acetate." *Id.* ¶ 51. Dr. Kirsch's contrary opinion in this case lacks credibility and should be disregarded.

Because Eagle's construction is the only one that adheres to the ordinary meaning ***and*** is consistent with the intrinsic evidence, it should be adopted.

C. "ADMINISTERING" LIMITATIONS

1. Par's Opening Position:

Eagle identified for construction several related claim limitations that each recite "administering" (in some instances "intravenously administering") either a "pharmaceutical composition" or a "unit dosage form" to a human patient. The parties' respective proposed constructions of these limitations is as follows:

Par's Proposed Constructions	Eagle's Proposed Constructions
"intravenously administering the pharmaceutical composition to the human" ('526 claim 1 (Ex. 3))	
Ordinary meaning, no construction necessary	"Intravenously administering the pharmaceutical composition to the human having the properties recited in the claim (does not permit dilution before administration)"
"intravenously administering the [portion/second portion] of the pharmaceutical composition to the human" ('223 claim 1 (Ex. 6))	
Ordinary meaning, no construction necessary	"Intravenously administering the portion of the pharmaceutical composition to the human having the properties recited in the claim (does not permit dilution before administration)"
"administering to the human a unit dosage form" ('478 claim 1 (Ex. 2); '209 claim 1 (Ex. 4))	
Ordinary meaning, no construction necessary	"Administering to the human a unit dosage form having the properties recited in the claim (does not permit dilution before administration)"

Par's Proposed Constructions	Eagle's Proposed Constructions
"administering the diluted unit dosage form to the human by intravenous administration" ('239 claim 1 (Ex. 1))	
Ordinary meaning, no construction necessary	"Administering the diluted unit dosage form generated by diluting the unit dosage form having the properties recited in the claim to the human by intravenous administration"

Eagle's proposed constructions of these "administering" claims simply parrot the language of the claims, and then, in the first three instances, seeks to insert yet another negative limitation, again by way of a parenthetical, stating that the claim "does not permit dilution before administration." Thus, the disputed issue with respect to these limitations is whether, in the first three instances, they should be construed by way of negative limitation to exclude administering the claimed vasopressin composition in the manner in which vasopressin compositions are nearly always administered—*i.e.*, in diluted form via continuous intravenous infusion. They should not.

a. A POSA Would Understand the "Administering" Limitations as Including Intravenously Administering the Claimed Vasopressin Compositions in Diluted Form

As is explained at length in the accompanying Declaration of Zlatan Coralic, injectable drug products intended for intravenous administration are oftentimes administered over an extended period of time via an "IV drip," in which the drug is

first diluted into an IV bag and administered into the patient's bloodstream over hours or days. Coralic Decl. (Ex. 20), ¶¶ 7-10.

That is exactly what the patents describe with respect to administering the disclosed vasopressin compositions. *Id.*, ¶¶ 16-17. Example 8, for example, is titled "Illustrative Regimen for Therapeutic Use of Vasopressin Formulation," and in the section subtitled "Preparation and Use of Vasopressin," the specification teaches that "[v]asopressin is provided at 20 units per mL of diluent, which is packaged as 1 mL of vasopressin per vial, and is diluted prior to administration," and that the "[v]asopressin is diluted in normal saline (0.9% sodium chloride) or 5% dextrose in water (D5W) prior to use to either 0.1 units/mL or 1 unit/mL for intravenous administration." '239 patent (Ex. 1), col. 22:18-67. It provides that "[v]asopressin is prepared according to TABLE 6 below":

TABLE 6

		Mix	
Fluid Restriction?	Final Concentration	Vasopressin	Diluent
No	0.1 units/mL	2.5 mL (50 units)	500 mL
Yes	1 unit/mL	5 mL (100 units)	100 mL

Id. at 22:18-67. Similarly, the patents also teach that "[a]ny formulation described herein can be diluted prior to administration to a subject." '526 patent (Ex. 3), col. 12:44-45.

The described regimen further provides that the vasopressin may be administered over extended periods of time, including in particular that:

> For post-cardiotomy shock, a dose of 0.03 units/minute is used as a starting point. For septic shock, a dose of 0.01 units/minute is recommended. If the target blood pressure response is not achieved, titrate up by 0.005 units/minute at 10- to 15-minute intervals. The maximum dose for post-cardiotomy shock is 0.1 units/minute and for septic shock 0.07 units/minute. After target blood pressure has been maintained for 8 hours without the use of catecholamines, taper vasopressin by 0.005 units/minute every hour as tolerated to maintain target blood pressure.

Id. at 60:27-36. The discussion of administering the specified amounts of vasopressin per minute for 8 hours, and then thereafter slowly tapering it off, indicates that it is describing continuous intravenous administration via an IV drip. Coralic Decl. (Ex. 20), ¶ 17.

Indeed, the patents disclose 73 additional exemplary methods of administering the claimed vasopressin compositions in accordance with "the present invention," spanning 24 columns of disclosures, which expressly recite diluting the claimed vasopressin compositions. *See, e.g.,* '526 patent (Ex. 3) at cols. 13-36.[27]

[27] The specifications then describe other similar embodiments that do not specifically mention diluting the vasopressin. '526 patent (Ex. 3), col. 36:48-45:59. There is nothing in the specifications, however, to indicate that the patentees intended those embodiments to *exclude* dilution of the vasopressin, and persons knowledgeable about the use and administration of vasopressin would not understand them as excluding dilution. Coralic Decl. (Ex. 20), ¶ 22 n.5. Rather, they would understand that those embodiments would cover administration of the vasopressin both in

By contrast, there is not a single example in the patents which specifically describes administering the claimed vasopressin compositions in concentrated form, without dilution. Thus, although a POSA would understand that vasopressin may be directly injected into the vein without dilution via an "IV push," he or she would also know that this method of administration is appropriate only in limited, exceedingly rare circumstances (that is, only when the patient is in active cardiac arrest—i.e., has no pulse). Coralic Decl. (Ex. 20), ¶¶ 14-15, 23.

Moreover, in each of the claims in which the disputed "administering" terms appear, the claim further recites that the administration must provide to the patient from about 0.01 to 0.1 units/minute of vasopressin.[28] Those rates convert to delivery of 0.002 mL/min to 0.02 mL/min, at the most, of vasopressin per minute. Coralic Decl. (Ex. 20), ¶ 27. Trying to administer such small amounts of a solution at that rate could be imprecise and potentially result in dosing errors and patient harm. *Id.*, ¶ 28. The recited dosage rate is readily achievable with precision, however, if the vasopressin is first diluted as described in the specification—i.e., is diluted in a standard IV bag using the ratios recited in Table 6. *Id.*

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concentrated form (such as via an IV push), or in diluted form (such as via an IV drip). *Id.*

[28] *See*, Ex. 1, '239 patent, claims 1 and 15; Ex.2, '478 patent, claim 1; Ex. 3,'526 patent, claim 1; Ex. 4, '209 patent, claim 1; Ex. 6, '223 patent, claims 1 and12.

Accordingly, POSAs reading the disputed claim terms as they appear in the context of the claims as a whole would immediately recognize that the claims encompass administration of the claimed vasopressin compositions in diluted form. *Id*.

b. Eagle's Proposed Constructions Improperly Exclude the Disclosed Methods of Administering Vasopressin Compositions

For the three instances of the "administering" limitations in which Eagle appends to its constructions the negative limitation by way of a parenthetical that the limitation "does not permit dilution before administration," Eagle's proposal would exclude from the claims the very method of administering vasopressin compositions expressly taught in the patents. That construction is misguided for a variety of reasons.

First, for the reasons discussed above, and as explained in detail in the Coralic Declaration (at ¶¶ 21-29), Eagle's construction is inconsistent with how a POSA would understand the "administering" limitations in the context of the claims as a whole. *See Interactive Gift Express, Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1332 (Fed. Cir. 2001) ("Throughout the construction process, it is important to bear in mind that the viewing glass through which the claims are construed is that of a person skilled in the art.").

Second, the Federal Circuit has repeatedly made clear that "[a] claim construction that 'excludes the preferred embodiment is rarely, if ever, correct and would require highly persuasive evidentiary support.'" *SynQor, Inc. v. Artesyn Tech, Inc.*, 709 F.3d 1365, 1378-79 (Fed. Cir. 2013) (citations omitted). Here, as described above, the preferred—and indeed only—method of administering the vasopressin compositions expressly taught in the patents is to administer them in diluted form. That is consistent with the way in which vasopressin products were being administered in nearly all circumstances at the time of the claimed inventions (i.e., any time the patient still had a pulse). Coralic Decl. (Ex. 20), ¶¶ 12-15. Eagle cites no evidence that the patentees intended to exclude that method from any of the claims of the patents-in-suit—let alone the "highly persuasive evidentiary support" required by *SynQor* and other Federal Circuit cases to exclude a preferred embodiment.

Third, under Eagle's proposed construction, the "administering" step of '526 claim 1 would be construed such that it "does not permit dilution before administration." Yet, claim 16 depends therefrom and specifically requires that the composition be "diluted in a diluent prior to administration to the subject." '526 patent (Ex. 3), claim 16. Eagle's construction would therefore render dependent claim 16 inoperable and nonsensical—the dependent claim would recite performing a step that the independent claim purportedly says is not permitted. Accordingly,

Eagle's proposed negative limitation cannot be correct. *See, e.g., Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1362 (Fed. Cir. 2008) (rejecting a claim construction that would render dependent claims meaningless); *Becton, Dickinson and Co. v. Tyco Healthcare Grp.*, 616 F.3d 1249, 1255 (Fed. Cir. 2010) ("A claim construction that renders claims facially nonsensical 'cannot be correct.'") (citations omitted).

In sum, POSAs reading the disputed terms, in the context of the claims as a whole and the teachings of the specification, would understand that except for those claims which expressly specify otherwise, "administering" the recited vasopressin compositions and dosage forms to a patient encompasses administering it in either diluted or undiluted form. For all of the above reasons, the Court should construe those terms to have that broad, ordinary meaning, and reject Eagle's attempt to exclude from the claims the preferred and only method of administration taught in the patents.

2. Eagle's Answering Position:

Par's brief and supporting ***extrinsic*** evidence clinical declaration spill much ink on establishing that physicians often administer vasopressin in diluted form, and the patent specifications describe exemplary methods involving dilution. But that misses the point. Indeed, Eagle does not dispute these facts. The same as Par and its clinical expert cannot, and do not, dispute that: (1) vasopressin can be, and often

is, administered in ***undiluted*** form; and (2) the patent specifications describe exemplary methods that do ***not*** involve dilution. *See* Par Op. Br. at 58–59 and 58 n.27; Ex. 20 (Coralic Decl.) ¶¶ 14–15, 27–28 and ¶ 22, n.5 (citing Ex. 3 ('526 patent) at 36:48–45:59); *see also* Ex. 4 ('209 patent) at 36:56–45:64; Ex. 6 ('223 patent) at 37:56–46:64. At base, however, Par's assertions address the wrong question. The issue for resolution here is not how vasopressin is most often used in practice, or what do the majority of the exemplary embodiments involve. Rather, it is what the "administering" claim terms mean in the context of the intrinsic evidence. As explained below, that evidence makes clear that claims that do not explicitly mention a dilution step before administration do not allow for a dilution step before administration.

a. The Patent Claims Support Eagle's Constructions

i. **Par's interpretation impermissibly reads out the claimed dosage form properties**

Par's uninformative "ordinary meaning" constructions ignore the plain language of the claims and inserts words into the claims where none exist. On the "administering" limitations, four of the asserted ('478, '209, '526 and '223) patents claim methods of treatment involving "administering" to a patient a "unit dosage form" or "pharmaceutical composition." Ex. 2 ('478 patent) at claim 1; Ex. 3 ('526 patent) at claim 1; Ex. 4 ('209 patent) at claim 1; and Ex. 6 ('223 patent) at claim

1.[29] The claims go on to state that "***the***" dosage form or composition that is administered to the patent has certain recited properties, including with respect to vasopressin concentration; pH; acetate buffer concentration; and impurity levels. Ex. 2 ('478 patent) at claim 1; Ex. 3 ('526 patent) at claim 1; Ex. 4 ('209 patent) at claim 1; and Ex. 6 ('223 patent) at claim 1. In contrast, while the claims of the '239 patent similarly describe a "unit dosage form," they then specifically require that the unit dosage form be diluted, provide parameters for such diluted form, and instruct that "***the diluted*** unit dosage form" must be administered. Ex. 1 ('239 patent) claim 1. For example, claim 1 of the '478 and '239 patents recite in relevant parts:

Claim 1 of the 478 patent	**Claim 1 of the '239 patent**
. . . the method comprising: **administering to the human a unit dosage form**, wherein **the unit dosage form consists essentially of**: a) from about 0.01 mg/mL to about 0.07 mg/mL of vasopressin . . . ; b) 10 mM acetate buffer; . . . **wherein: the unit dosage form** has a pH of 3.8; the administration provides to the human from about 0.01 units of	. . . the method comprising: a) providing a pharmaceutical composition for intravenous administration consisting of, in ***a unit dosage form***: i) from about 0.01 mg/mL to about 0.07 mg/mL of vasopressin . . . iv) 0-2% vasopressin degradation products; . . . b) ***diluting the unit dosage form in a diluent*** to provide a concentration from

[29] The asserted claims use both "unit dosage form" and "pharmaceutical composition," depending on the patent. *Compare, e.g.*, Ex. 2 ('478 patent) claim 1 ("unit dosage form") *with, e.g.*, Ex. 3 ('526 patent) claim 1 ("pharmaceutical composition"). For the purposes of construing these claim terms, the phrases are functionally equivalent and any reference to "unit dosage form" is equally applicable to "pharmaceutical composition."

vasopressin . . . thereof per minute to about 0.1 units of vasopressin . . . per minute . . .	about 0.1 units/mL to about 1 unit/mL of vasopressin . . . ; and c) ***administering the diluted unit dosage form*** to the human by intravenous administration; wherein: the unit dosage form has a pH of 3.5 to 4.1; the administration provides to the human from about 0.01 units of vasopressin . . . per minute to about 0.1 units of vasopressin . . . per minute. . .

Ex. 2 ('478 patent) at claim 1 (emphasis added); Ex. 1 ('239 patent) at claim 1 (emphasis added). Eagle's reading of these claims is straightforward: one must administer ***the*** "unit dosage form" for the claims that provide as such, and administer "***the diluted*** unit dosage form" for the claims of the '239 patent. Relying heavily on extrinsic evidence, Par, however, insists upon inserting words into the claims of each patent. It argues that even for the claims that do not provide for dilution, one must ***automatically assume*** dilution, thereby effectively eradicating any difference between the claims that do not provide for dilution and the '239 patent claims.

One of the fundamental rules governing claim construction is that "[i]n construing claims, the analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to 'particularly point out and distinctly claim the subject matter which the patentee regards as his invention.'" *Interactive Gift Exp.*, 256 F.3d at 1331. Thus,

courts must "construe claims with an eye toward giving effect to all of their terms." *Haemonetics Corp. v. Baxter Healthcare Corp.*, 607 F.3d 776, 781 (Fed. Cir. 2010) (citing *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006)). As part of this analysis, the antecedent basis for a particular element must be maintained. *See, e.g.*, *id.* at 781–82. Notably, this is the case "even if [the construction] renders the claims inoperable or invalid." *Id.* at 781.

For example, in *Haemonetics*, the claim at issue recited "[a] centrifugal unit comprising a centrifugal component and a plurality of tubes," with "***the centrifugal unit*** . . . having a radius between 25 and 50 mm and a height between 75 and 125% of the radius." *Id.* at 780. In reversing the district court, the Federal Circuit held that the recited dimensions must apply to the "centrifugal unit" as a whole and ***not*** the constituent "centrifugal component." *Id.* at 781–82. Any other construction would "ignore[] the antecedent basis for 'the centrifugal unit,' and fail[] to give effect to the claim language "comprising a centrifugal component.'" *Id.* at 782 (citations omitted). In reaching this conclusion, the Federal Circuit rejected the patentee's argument that such a construction would be "nonsensical[]," would "exclude[] every embodiment in the specification" and would "ignore[] … the invention's goals." *Id.* at 781.

Here, the asserted claims of the '478, '209, '526 and '223 patents make clear that it is "***the*** unit dosage form" or "***the*** pharmaceutical composition" with the

properties recited in the claim that is "administer[ed]" to the patient. *See supra*. Dilution of the recited unit dosage form would result in a ***different*** unit dosage form with a ***different*** vasopressin concentration, ***different*** acetate buffer concentration, and ***different*** pH from that recited in the claims. Ex. 25 (Amiji Decl.) ¶ 34. For example, at the smallest 20:1 dilution cited by Par in its opening positon, a dosage form with 0.07 mg/mL vasopressin content, 10 mM acetate buffer concentration and pH of 3.8, as recited in the '478 patent claim 1, would be watered-down to approximately 0.0035 mg/mL vasopressin content, approximately 0.5 mM acetate buffer, and a higher pH. *Id.* ¶¶ 35–41; *see also* Par Op. Br. at 57. Thus, under Par's proposed reading—contrary to the express textual instruction provided in the claims—"***the*** unit dosage form" or "***the*** pharmaceutical composition" would not be administered at all. Instead, a materially different formulation with properties ***outside the claimed limitations*** would be administered. Under these circumstances, to give meaning to the claims terms, it must be "***the*** unit dosage form" or "pharmaceutical composition" with the recited properties that is administered to the patent.

ii. **Claim differentiation further supports Eagle's Construction**

Claim differentiation between the claims of the '478, '209, '526 and '223 patents on the one hand, and claims of the related '239 patent on the other, further precludes Par's proposed construction to allow dilution before administration. *See,*

e.g., *Chrimar Holding Co. v. ALE USA Inc.*, 732 F. App'x 876, 884 (Fed. Cir. 2018), as amended (June 1, 2018). Under Par's proposed construction, the dilution limitations of the '239 patent—which are limitations added during prosecution that were ***dispositive*** to Par's overcoming the Patent Office's obviousness rejection—would be improperly rendered superfluous, as Par reads them into each asserted claim regardless.

Chrimar Holding is instructive. In that case, the Federal Circuit reversed the district court's decision finding the term "adapted to" to have a broad plain meaning that effectively rendered the term as a non-limitation. *Id*. at 883. In so holding, the Federal Circuit noted that the term must not be rendered meaningless in part because the term appeared only in the patent at issue, but "not the other patents involving essentially the same specification, suggesting that the claim scope chosen for the asserted claims in th[at] patent is only a subset of what the specification may support." *Id.* at 883–84. Thus, the Federal Circuit reversed the district court and adopted a proposed construction that provided a meaningful limitation to the scope of the claims at issue.

Here, as noted above, the claims of the '478, '209, '526 and '223 patents recite "administering" a "unit dosage form" or "pharmaceutical composition" having certain recited properties. *See* Section II.C.2.a.i, *supra*. The '239 patent, in contrast, claims a method involving "***providing***" a "unit dosage form" having certain recited

properties, "***diluting*** the unit dosage form," and "administering the ***diluted*** unit dosage form" to the patient. Ex. 1 ('239 patent) claim 1. This difference is no accident. Rather, Par amended the '239 patent claims to add the dilution step during prosecution to overcome prior art that included the same properties as the recited unit dosage form but purportedly "fail[ed] to teach or suggest [the added dilution step] because ***no reference suggests dilution of a vasopressin formulation prior to administration***." Ex. 10 (Response to Final Office Action (Appl. No. 14/717,877 ('239 Patent)) (Nov. 3, 2016)) at 7. It made no such amendment to the '478, '209, '526 and '223 patent claims.

The patentees thus clearly knew how to claim a method involving diluting a unit dosage form ***before*** administering. That they did so only in some of the asserted patents indicates that they did not contemplate a dilution step unless explicitly stated in the claims. *Chrimar Holding*, 732 F. App'x 876 at 883–84.

iii. **Dependent claim 16 of the '526 patent cannot broaden the scope of claim 1**

Par's citation to dependent claim 16 of the '526 patent is unavailing. That claim recites "[t]he method of claim 1, wherein the pharmaceutical composition is diluted in a diluent prior to administration to the subject." Ex. 3 ('526 patent) claim 16. That claim language confirms that the patent uses the term "administration" to mean actually giving the composition to the patent. Thus, claim 16, as well as claim 17 that depends on it, provides for "administration" to a patient of a composition that

does not meet the vasopressin concentration requirements of claim 1. *See id.* For example, claim 17 would permit "administration" to the patent of a composition with "about 0.21μg/mL to about 2.1 μg/mL of vasopressin," which falls entirely outside of the range of claim 1. *Id.* claim 17. Thus, as Par concedes, claims 16 and 17 of the '526 patent would *broaden* the scope of claim 1. *See* Par Op. Br. at 61–62.

The Federal Circuit has held that, although "dependent claims can aid in interpreting the scope of claims from which they depend, they are only an aid to interpretation and are not conclusive." *See, e.g.*, *Baxalta Inc. v. Genentech, Inc.*, C.A. No. 17-509-TBD, 2018 WL 6304351, at *11 (D. Del. Dec. 3, 2018) (Dyk, J.) (quoting *Regents Univ. of Cal. v. Dakocytomation Cal., Inc.*, 517 F.3d 1364, 1375–76 (Fed. Cir. 2008)). Thus, "[t]he retention of inconsistent language in the dependent claims does not suggest that the interpretation of independent claims should depart from the original meaning of the[ir] term[s]." *Id.* In particular, "it would be inappropriate to use the doctrine of claim differentiation to broaden [the independent claim] to include a limitation imported from a dependent claim." *See, e.g.*, *Enzo Biochem Inc. v. Applera Corp.*, 780 F.3d 1149, 1156–57 (Fed. Cir. 2015). This is because "dependent claims cannot broaden an independent claim from which they depend." *Id.*

In *Enzo*, for instance, the Federal Circuit held that the plain meaning of an independent claim term in the context of the intrinsic evidence covered only a

method of "indirect detection" of DNA hybridization, rather than both indirect and direct detection. *Enzo Biochem*, 780 F.3d at 1154–56. That was despite the fact that a dependent claim recited use of "direct" detection. *See id.* at 1156–57. A similar result was also reached by this court in *Baxalta*, as the claim language, specification, and prosecution history supported a construction of "antibody" that excluded the broader usage of the term in the dependent claims. *See Baxalta*, 2018 WL 6304351, at *11. In fact, "the Federal Circuit has held that the failure of a patentee to conform dependent claims to the scope of the independent claims results in invalidation of the inconsistent claims rather than an expansion of the independent claim." *Id.* (citing *Dakocytomation*, 517 F.3d at 1375–76). Thus, the proper finding here is that claims 16 and 17 of the '526 patent are invalid, not that they allow Par to overcome the plain meaning of the claims and its prosecution statements.

Par's cited authorities do not alter these rules of law and are inapposite here. *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1362 (Fed. Cir. 2008), considered whether to afford the term "and" conjunctive or disjunctive meaning. The Court chose the latter because that was supported by the specification as well as usage in the dependent claims. *Id.* Here, in contrast, Eagle's construction is the only possible interpretation that gives full effect to each and every term regardless of the dependent claims, and *Ortho-McNeil* itself recognizes that Par's attempt to rewrite the claims is impermissible. *See id.* at 1362 ("[C]ourts may not

redraft claims, whether to make them operable or to sustain their validity. Even 'a nonsensical result does not require the court to redraft the claims of the . . . patent.'" (alteration in original) (citation omitted)).

Par's other authority, *Becton, Dickinson and Co. v. Tyco Healthcare Grp.*, 616 F.3d 1249, 1255 (Fed. Cir. 2010), also does not support its position here. Foremost, *Becton* did not even consider how dependent claims may or may not inform the construction of independent claims. *See id.* at 1255. The "nonsensical" result Par alludes to in fact refers to a construction that would have interpreted a single structure to satisfy two claim elements, a "physical impossibility," that was inconsistent with both the intrinsic evidence and the law. *See Id.* Even Par and its expert admit that there is no "physical impossibility" here. *See* Par Op. Br. 58–59, 60–61; Ex. 20 (Coralic Decl.) ¶¶ 14–15, 27–28.

b. The Patent Specifications Support Eagle's Constructions

The patent specifications further confirm that the claims mean what they plainly say. All disclose dilution as an option, never teaching that such a method is required or even desirable. For example, the patents teach that vasopressin formulations "***can*** be diluted," *e.g.*, Ex. 3 ('526 patent) at 12:44–45 (emphasis added), not that dilution is necessary or even typical. And Par acknowledges that the patents describe two almost identical methods of treating patients using vasopressin formulations: one with a dilution step and one without. *See* Par Op. Br.

at 58–59 and 58 n.27; *see also, e.g.*, Ex. 3 ('526 patent) at 36:48–45:59); Ex. 4 ('209 patent) at 36:56–45:64; Ex. 6 ('223 patent) at 37:56–46:64. Par does not explain why the patent would need to describe both methods if dilution was actually contemplated, much less necessary, in both. *See, e.g.*, *Sanofi-Aventis*, 2018 WL 389183, at *5–6 ("The specifications do not appear to use the words 'thread' and 'spline' interchangeably . . . . There is no reason to conclude that the patents use the word 'spline' to refer to a type of 'thread.'").

Thus, not only did the patentees know how to claim administering a diluted dosage form that differs from the properties recited, but they also knew how to describe it. By omitting the described diluted dosage forms from the claims, however, Par informed the public that such a method was outside the scope. *See, e.g.*, *Aptalis Pharmatech, Inc. v. Apotex Inc.*, 718 F. App'x 965, 970 (Fed. Cir. 2018); *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1290 (Fed. Cir. 2009).

Aptalis is instructive. There, the asserted patent described the use of a noncontinuous water-impermeable coating, with "apertures exposing between about 5-75%" of the coated core, but claimed only a coating that "surround[ed] said core." *Aptalis*, 718 F. App'x at 970. The Federal Circuit concluded that, in light of "the inventors' ability to describe a non-continuous coating when they so desired," the "decision to claim a coating that surrounds the core instead of claiming a coating with a certain percentage of exposed core surface would have informed a person of

ordinary skill in the art that the claims require a continuous coating." *Id.* This is exactly what the patentees chose here by describing the administration of diluted dosage forms but failing to claim it.

Beyond these disclosures, Par tellingly ignores additional disclosures indicating that dilution is not suggested automatically by the asserted claims. After disclosing the alternative methods of treatment, the patents also teach that a wide range of concentrations and volumes could be used for the therapeutic product. Specifically, the specification informs POSAs that "[p]harmaceutical compositions of the invention can be formulated in any suitable volume," ranging from "about 0.1 mL" to "about 10 mL." *See, e.g.*, Ex. 1 ('239 patent) at 8:52–9:12; *see also, e.g.*, Ex. 2 ('478 patent) at 8:34–59 (same); *see also* Ex. 25 (Amiji Decl.) ¶ 43. The patents teach that "[a] therapeutically-effective amount of a compound described herein can be present in a composition at a concentration of, for example, about 0.1 units/mL . . . [to] about 50 units/mL" or from "about 0.001 mg/mL" to "about 10 mg/mL." *See, e.g.*, Ex. 1 ('239 patent) at 9:13–28; *see also, e.g.*, Ex. 2 ('478 patent) at 8:60–9:8 (same); *see also* Ex. 25 (Amiji Decl.) ¶ 43. Nothing in these disclosures links any of these volumes or concentrations to dilution, including to achieve any particular administration rate. *See id.* Instead, the patent teaches that ***any*** of these volumes are suitable for use in the claimed methods, regardless of whether any dilution is used.

Par contends that Eagle's construction would exclude "the preferred—and indeed only—method of administering vasopressin compositions taught in the patents." As Par itself recognizes, however, the patents disclose that dilution is optional and include nine columns of detailed "embodiments that do not specifically mention diluting the vasopressin." Par Op. Br. at 58 n.27. "[W]here the patent describes multiple embodiments, every claim does not need to cover every embodiment." *Pacing Techs., LLC v. Garmin Int'l, Inc.*, 778 F.3d 1021, 1026 (Fed. Cir. 2015). Indeed, the patentee may "pick[] out one among several embodiments, especially where other claims (perhaps in the same or related patents) claim more broadly or focus on other embodiments." *Chrimar Holding*, 732 F. App'x at 884. This is precisely what Par did here by obtaining one set of patents that are directed to administration of ***the*** unit dosage form, and another patent for the administration of ***the diluted*** unit dosage form. Thus, to the extent Par's cited *SynQor* case supports requiring "highly persuasive evidentiary support" for a construction, it is only where it would exclude ***all*** recited embodiments, not where the patentee picked out a specific embodiment to claim among several different embodiments.

Furthermore, even assuming *arguendo* that Eagle's construction did exclude ***all*** claimed embodiments, there is more than ample evidence supporting such exclusion. The Federal Circuit has repeatedly held that "the unambiguous language of the amended claim controls over any contradictory language in the written

description." *Elekta Instrument S.A. v. O.U.R. Sci. Int'l, Inc.*, 214 F.3d 1302, 1308 (Fed. Cir. 2000). Accordingly, "court[s] must not allow the disclosed embodiment to 'outweigh the language of the claim, especially when the court's construction is supported by the intrinsic evidence.'" *Rolls-Royce, PLC v. United Techs. Corp.*, 603 F.3d 1325, 1334 (Fed. Cir. 2010) (citation omitted). Because it is the claim language that controls, parties may not "rewrite the express claim language" "in order to correct claims that are inconsistent with the specification." *MiiCs & Partners Am., Inc. v. Toshiba Corp.*, C.A. No. 14-803-RGA, 2016 WL 4573103, at *16–17 (D. Del. Aug. 31, 2016). Instead, where the clear claim language and prosecution history support such a construction, the preferred embodiments should be excluded. *See, e.g.*, *id.*; *Rembrandt Diagnostics, L.P. v. Innovacon, Inc.*, 2017 WL 6059129, at *4 (S.D. Cal. Dec. 7, 2017); *Rolls-Royce*, 603 F.3d at 1334. Here, Eagle's proposed construction does not read out all preferred embodiments, but even if it did, that would be justified here.

c. Par's Prosecution Statements Support Eagle's Construction

Par's arguments before this Court are directly contrary to those it made before the Patent Office in order to obtain the '239 patent at issue here. There, Par argued that prior art disclosures of dosage forms with essentially identical properties to those recited in the claims did not teach, or even render obvious, dilution before administration ***unless specifically disclosed.***

Specifically, Par sought to overcome rejections based on two references—Treschan and PPC—which disclosed intravenous vasopressin formulations for increasing blood pressure as claimed. Ex. 10 (Response to Final Office Action (Appl. No. 14/717,877 ('239 Patent)) (Nov. 3, 2016)) at 7–8; Ex. 25 (Amiji Decl.) ¶ 44–45; *see also* Ex. 28 (T. Treschan et al., The Vasopressin System, Physiology and Clinical Studies, *Anesthesiology* 105(3):599–606 ("Treschan")); Ex. 29 (Pharmaceutical Partners of Canada Inc., Vasopressin Injection, USP, June 2009 ("PPC")). And both disclosed substantially identical vasopressin formulations having substantially identical properties as recited in the claims. Ex. 25 (Amiji Decl.) ¶ 44; *see also* Ex. 28 (Treschan) at 599, 605 (Table 4); Ex. 29 (PPC). Yet neither specifically made any reference to dilution of a vasopressin formulation prior to administration.

In response to this rejection, Par amended the claims "to recite c) diluting the unit dosage form in a diluent to provide a concentration from about 0.1 units/mL to about 1 unit/mL of vasopressin or the pharmaceutically-acceptable salt thereof; and d) administering the diluted unit dosage form to the human by intravenous administration." Ex. 10 (Response to Final Office Action (Appl. No. 14/717,877 ('239 Patent)) (Nov. 3, 2016)) at 7. Par then argued that Treschan and PPC "fail to teach or suggest every element of the claims as amended herewith at least because ***no reference suggests dilution of a vasopressin formulation prior to***

administration." *Id.* (emphasis added). They renewed this argument several months later in an interview with the examiner, stating expressly "that the amendment includes a new dilution step to 0.1 units/ml to 1 unit/ml to distinguish the claims from the prior art which teaches that the compound is supplied at 20 U/ml and does not require dilution." Ex. 9 (Applicant-Initiated Interview Summary (Appl. No. 14/717,877 ('239 Patent)) (Sept. 9, 2016)) at PAR-VASO-0008681. Thus, before the PTO, the patentees argued unequivocally and repeatedly that there must be a specific instruction to a POSA to dilute a dosage form with the recited characteristics and to administer that diluted dosage form in order to teach this particular method or even to render it obvious.

Here, in contrast, Par argues that "POSAs reading the disputed claim terms as they appear in the context of the claims as a whole would immediately recognize that the claims encompass administration of the claimed vasopressin compositions in diluted form." Par Op. Br. at 60. In fact, Par's expert, Dr. Coralic, goes as far as to state that "[f]or ***any*** patients coming to a hospital . . . who had a pulse, vasopressin would be administered to them via an IV drip" and that this was well-known based on the prior art. Ex. 20 (Coralic Decl.) ¶ 13. Dr. Coralic's description of the state of the art, if true, would have applied equally to the prior art vasopressin formulations that Par distinguished during prosecution, which otherwise had nearly identical properties:

PRIOR ART (Treschan/PPC)	Parameter	ASSERTED PATENTS
Hypotension	**Use**	Hypotension
0.01–0.04, 0.1	**Dose (U/min)**	0.01–0.1
0.038	**Vasopressin (mg/mL)**	0.01–0.07
2.5–4.5	**pH**	3.5–4.1

See Ex. 25 (Amiji Decl.) ¶ 44; *see also* Ex. 28 (Treschan) at 599, 605 (Table 4); Ex. 29 (PPC). Par argues that "the viewing glass through which the claims are construed is that of a person skilled in the art." *Interactive Gift Express*, 256 F.3d at 1332 (cited in Par Op. Br. 60). But obviousness—the rejection Par sought to overcome—is of course viewed through the same lens: that of a POSA. *E.g.*, *Graham v. John Deere Co.*, 383 U.S. 1 (1966). Par and its expert provide no reason as to why a POSA, faced with the claimed method of use and vasopressin formulations, would now find dilution to be an automatically assumed and well-understood step, when they previously stated that the same method of use and vasopressin formulations in the prior art would not even render a dilution step obvious. In short, Par's construction ***renders superfluous*** the very claim limitation that Par itself specifically added during prosecution to overcome prior art, which was ***essential*** for securing the '239 patent. Ex. 10 (Response to Final Office Action (Appl. No. 14/717,877 ('239 Patent)) (Nov. 3, 2016)) at 7.

Instead of addressing this inconsistency, Par and its expert make sweeping statements about how and why a POSA would immediately know that dilution is

contemplated by claims reciting the undiluted dosage form only. But that equally would apply to the prior art as well, contrary to Par's prosecution statements. For example, Par, as background, represents repeatedly that "[h]istorically, vasopressin products have been sold as injectable products . . . intended for intravenous administration" and that this drug "is administered in almost all instances via continuous intravenous administration using an IV drip, in which the vasopressin is diluted before use." Par Op. Br. at 2. Par doubled-down on this statement to add that that dilution "is consistent with the way in which vasopressin products were being administered in nearly all circumstances at the time of the claimed inventions." *Id.* at 61. These statements are parroted and supported by its expert as well. Ex. 20 (Coralic Decl.) ¶¶ 10–15. Of course, if this background would be known by a POSA for the purposes of interpreting the claim as of the priority date, as Par argues, then this same information would have been known to a POSA for the purposes of evaluating validity, as before the Patent Office. Thus, this purported "[h]istorical[]" preparation and use of vasopressin "in nearly all circumstances" should lead to the same conclusion based on the prior art, such that the POSA would immediately recognize that the prior art formulations would be recognized. Par makes no attempt to reconcile this discrepancy and explain why it believes a POSA would have deviated from the purported preexisting practice of diluting vasopressin products in

the context of the art. Either Par deliberately misled the Patent Office to secure the claims, or it is wrong now.

Turning to the specific method claimed, Par again identifies no reason why a POSA would act differently based on the prior art and claims. Par now argues that a POSA would know that administration without dilution "is appropriate only in limited, exceedingly rare circumstances (that is, only when the patient is in active cardiac arrest—i.e., has no pulse)." Par Op. Br. at 59; Ex. 20 (Coralic Decl.) ¶ 14. In support of this argument, Par relies on its expert declaration, which in turn cites to an article from 2010, *id.*, *i.e.*, prior art, that would have similarly informed a POSA's analysis in the obviousness context.

Par also argues that "[t]he recited dosage rate is readily achievable with precision, however, if the vasopressin is first diluted," something a POSA would know and prefer to administering an undiluted formulation. Par Op. Br. at 59. According to Par, a POSA would know that the recited dose of "0.01 to 0.1 units/minute of vasopressin" would be difficult to achieve because such administration "could be imprecise and potentially result in dosing errors and patient harm." Par Op. Br. at 59. Again, these very dose and concentration parameters were disclosed in the prior art Par distinguished. Ex. 10 (Response to Final Office Action (Appl. No. 14/717,877 ('239 Patent)) (Nov. 3, 2016)) at 7; *see also* Ex. 28 (Treschan) at 599, 605; Ex. 29 (PPC). Furthermore, Treschan does not teach the "IV push"

method for the aforementioned clinical use that Par and its expert contend is the alternative to administering a diluted dosage form. Par Op. Br. 58–59; Ex. 20 (Coralic Decl.) ¶¶ 11, 14–15, 23. This further confirms the inconsistency between Par's statements to the Patent Office and its representations to this Court. Neither Par nor its expert cite ***any*** supporting information in the patents or even any other reference for these assertions or identify any new knowledge that the POSA would not already have possessed from the prior art.

In short, Par is trying to have it both ways and, depending on whether it is addressing validity or infringement, have the hypothetical POSA reach its desired, but contrary, conclusions. Par's POSA knows nothing of intravenous administration or dilution for the purposes of validity, but suddenly remembers a wealth of universal knowledge when faced with the ***same exact formulation and dosing parameters***. This position is fundamentally unfair and vitiates the public notice function of the intrinsic record, contrary to established, black-letter law. A "patent may not, like a nose of wax, be twisted one way to avoid anticipation and another to find infringement." *01 Communique Lab., Inc. v. Citrix Sys., Inc.*, 889 F.3d 735, 743 (Fed. Cir. 2018) (quotation omitted).

d. Par's Extrinsic Evidence Declaration Cannot Overcome The Overwhelming Intrinsic Evidence

Faced with this overwhelming intrinsic evidence, Par is forced to rely on ***extrinsic*** evidence in the form of a litigation-motivated expert declaration that

contradicts its prosecution statements. But such extrinsic evidence cannot overcome the overwhelming contrary ***intrinsic*** evidence. *See Interactive Gift Expres*, 256 F.3d at 1332 ("Relying on extrinsic evidence to construe a claim is 'proper only when the claim language remains genuinely ambiguous after consideration of the intrinsic evidence.'" (citation omitted)).

Furthermore, its positions in reliance on that extrinsic evidence are unavailing. As with the rejected arguments of the patentee in *Haemonetics*, Par's and its expert's assertions that Eagle's proposed construction would read out many of the exemplary embodiments, and "***could***" lead to a method that is "***imprecise*** and [could] potentially result in dosing errors and patient harm" are irrelevant.

As an initial matter, as discussed above, Par concedes that at least some of the disclosed embodiments involve administering vasopressin dosage forms without dilution. Par Op. Br. at 58 n.27. Dr. Coralic similarly concedes that vasopressin dosage forms do not necessarily need to be diluted before administration. Ex. 20 (Coralic Decl.) ¶¶ 14–15, 27–28 and ¶ 22, n. 5. Nor does Par or Dr. Coralic assert that performing the method according to Eagle's construction would be impossible, only that it "***could***" be "***imprecise***." Par Op. Br. at 59; Ex. 20 (Coralic Decl.) ¶¶ 27–28; *see also* Ex. 25 (Amiji Decl.) ¶ 42. That "[t]he recited dosage rate is ***readily achievable with precision***, however, if the vasopressin is first diluted," Par Op. Br. at 59, does not warrant rewriting the claims. Indeed, even if Eagle's construction

rendered the claims wholly inoperable—which Par and its expert have not established—that still would not justify Par's proposed rewrite. *See Haemonetics*, 607 F.3d 776; *cf. Chef Am., Inc. v. Lamb–Weston, Inc.*, 358 F.3d 1371, 1374 (Fed. Cir. 2004) ("[W]here, as here, claims are susceptible to only one reasonable interpretation and that interpretation results in a nonsensical construction of the claim as a whole, the claim must be invalidated.").

At base, Eagle's proposed construction is the only one that is supported by all of the intrinsic evidence, including the claim language, the specifications and Par's prosecution statements. Par's construction, in contrast, is not even supported by the extrinsic evidence it is forced to rely upon. Eagle's construction should be adopted.

3. Par's Reply Position:

a. Eagle's Construction Is Based on its Erroneous Interpretation of the Word "The"

All of Eagle's arguments turn on its interpretation of the word "the"—according to Eagle and its putative expert, because the disputed "administering" steps refer to administering "the" composition (or unit dosage form) recited earlier in the claims,[30] they necessarily must be construed as excluding the administration

[30] As noted above, some claims refer to a "pharmaceutical composition," while others use the term "unit dosage form." Eagle asserts that the two are functionally equivalent for purposes of construing the claims, such that any reference in their arguments to one applies equally to the other. *See supra* at 64 n.29. Consistent therewith, and for purposes of simplicity, Par shall refer to vasopressin "compositions" or "pharmaceutical compositions," with the understanding that its

of that composition in diluted form. *See* Section 2.a.i above; Ex. 25 (Amiji Decl.) ¶¶ 34, 41. That argument, however, is contrary to both the most natural reading of the claims, and the way the claims would be understood by a POSA.

Claim 1 of the '526 patent, for instance, recites "providing a pharmaceutical composition" containing specified amounts of vasopressin and other components, and thereafter "administering the pharmaceutical composition" to a patient. Ex. 3 ('526 patent), claim 1. The recited vasopressin compositions can be "administered" in a variety of ways, including among others: (1) via continuous intravenous infusion, in which the composition is first diluted in an IV bag before being infused into the patient, or (2) via direct injection, without dilution, via an IV push. Ex. 20 (Coralic Decl.) ¶¶ 12-17. [31] In both of those instances, "the" vasopressin compositions are being "administered" to the patient.

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arguments apply with equal force and in the same manner to any claims that refer instead to "unit dosage forms."

[31] Eagle derisively refers to Dr. Coralic's Declaration as "litigation-motivated" (*supra* at 82), which is quite ironic given that Eagle's expert (Dr. Amiji) largely just regurgitates Eagle's legal arguments (i.e., interpreting the prosecution history, talking about concepts of obviousness, etc.), with little pretense of providing actual scientific or technical information within the scope of his expertise. By contrast, Dr. Coralic focused on providing the Court with background information concerning how vasopressin compositions have been and are being administered to patients and his perspective, as one experienced in the use and administration of vasopressin, on how the disputed "administering" limitations fit within the context of the claims as a whole.

Consider, for example, the following hypothetical. A patient suffering from septic shock arrives by ambulance at the emergency room of a hospital. An ER doctor examines the patient upon arrival, and determines that she should be given 20 units of vasopressin to increase her blood pressure. The doctor thereafter provides a fellow clinician (i.e., a nurse, clinical pharmacist, physician's assistant, or other attending healthcare professional) with a 1 mL vial containing an aqueous solution of 20 units of vasopressin,[32] and instructs the clinician to administer "the" vasopressin composition to the patient.

In those circumstances, the clinician would assess the situation, make a determination as to whether circumstances warranted that "the" vasopressin composition be administered via an IV drip (*i.e.*, after being diluted in an IV bag) or an IV push (*i.e.*, without dilution), and then proceed accordingly. Ex. 33 (Suppl. Coralic Decl.) ¶ 8. Either way, the clinician will have administered "the" vasopressin composition provided and thereby complied with the doctor's instructions to administer "the" vasopressin composition to the patient. *Id.* ¶ 9.

[32] One mg of vasopressin is equivalent to 530 units. *See* Ex. 3 ('526 patent), at col. 62:10. Thus, 20 units of vasopressin in a 1 mL solution converts to 0.0377 mg/ml of vasopressin, which is within the range of "from about 0.01 mg/mL to about 0.07 mg/mL of vasopressin" in each of the "pharmaceutical compositions" and "unit dosage forms" recited in the disputed claims.

Thus, the most natural reading of the term "administering ***the*** pharmaceutical composition [or unit dosage form]," as recited in the claims at issue, is that it encompasses administration of the recited composition via either an IV drip (with dilution) or an IV push (without dilution). In those instances where an IV drip is used, the concentrations of the vasopressin and other components will have changed during the administration process when the composition was diluted in the IV bag, but that does not change the fact that the composition originally "provided" to the clinician will have been "administered" to the patient.

According to Eagle, in circumstances where an IV drip is used, even though "***the*** pharmaceutical composition" packaged in the vial is extracted from the vial and thereafter infused in its entirety into the patient's bloodstream, it was not administered to the patient. That is nonsensical.

Thus, while claim 1 of the '239 patent specifically requires dilution (and thus would not encompass administration of "the" composition without dilution, such as via an IV push), a person knowledgeable about the use and administration of vasopressin products would understand that the remaining claims at issue encompass administering "the" recited vasopressin "pharmaceutical compositions" and "unit dosage forms" in either diluted or undiluted form. *Id.* ¶ 12.[33]

[33] Eagle's expert witness asserts that this reading of the claim renders them "textually and internally [in]consistent." Ex. 25 (Amiji Decl.) ¶ 41; *see also id.* ¶ 34. He has a Ph.D. in Pharmaceutical Science/Pharmaceutics, however, not linguistics.

Eagle asserts that under Par's arguments, "one must ***automatically assume dilution***, thereby effectively eradicating any difference between the claims that do not provide for dilution and the '239 claims." *Supra* at 65 (emphasis in original). Par argues no such thing—its argument is that the disputed claims are broader than those of the '239 patent. Whereas the '239 patent claims were narrowed during prosecution to expressly recite a dilution step and require that the vasopressin composition be administered in diluted form, there is nothing in the remaining claims that restricts the manner in which they are administered, such that they encompass administering "the" vasopressin composition with or without dilution.[34]

b. Eagle's Construction Is Inconsistent with Its Earlier Contentions

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Moreover, he does not profess to have any knowledge or experience in the administration of vasopressin compositions, and for the reasons just described, there is nothing inconsistent in construing the broad, general term "administering" to encompass all forms of administering the claimed vasopressin compositions, including via an IV drip, as well as via an IV push.

[34] The only case on which Eagle relies in this section of its Answering Position—*Haemonetics Corp. v. Baxter Healthcare Corp.*, 607 F.3d 776 (Fed. Cir. 2010)—is of no help to Eagle. In *Haemonetics*, the court held that the phrase "*the* centrifugal unit" necessarily referred back to the "centrifugal unit" recited earlier in the claim at issue. *Id.* at 782. Here, there is no dispute that terms "*the* pharmaceutical composition" and "*the* unit dosage form" refer back to the "pharmaceutical compositions" and "unit dosage forms" recited in the earlier "providing" steps of the disputed claims. Eagle errs, however, by thereafter making the further leap that administering "the" composition (or unit dosage form) cannot encompass administering it in diluted form. That leap is unsupported by the language of the claims, anything in the intrinsic evidence, or any case law.

Although Eagle now argues that its proposed construction is the only possible reading that is consistent with the language of the claims, it is actually a construction that Eagle dreamt up only recently.

If the Court were to construe the disputed "administering" limitations as precluding dilution, Eagle undoubtedly will argue that it does not infringe the four patents-in-suit that include those limitations. [redacted].

Then, in this litigation, Eagle at first reiterated those some positions. When asked via interrogatory to provide its non-infringement and invalidity positions, Eagle responded by pointing back to its Paragraph IV Notice, which it incorporated

[35] *See* D.I. 1 (Complaint), ¶¶ 11-13, 29-30.

into its responses. *See* Ex. 35 (Excerpts of Rog Response) at 5-9. Thus, at that time, Eagle was still reading the claims as allowing dilution, not precluding it, [redacted]

Eagle's earlier assertions directly contradict the claim construction arguments it is now making.[36] It was only sometime in the last few months that Eagle suddenly realized that the "only possible" reading of the disputed "administering" limitations is that they preclude dilution. The Court should recognize Eagle's proposed construction for what it is—a recently dreamt up, lawyer-driven reading of the claims that contradicts how the claims would be understood by laypersons and POSAs alike.

c. Adopting Eagle's Construction Would Violate Well-Established Canons of Claim Construction

As Par demonstrated in its opening brief, reading the disputed claims as precluding dilution would violate at least two fundamental canons of claim construction—namely, that a construction that excludes the preferred embodiment

[36] One mg of vasopressin is equivalent to 530 units. *See* Ex. 3 ('526 patent), at col. 62:10. [redacted]

is "rarely, if ever, correct" (*SynQor*, 709 F3d at 1378-79), and that claims should not be construed so as to render dependent claims meaningless (*Ortho-McNeil*, 520 F.3d at 1362).

In response, Eagle does not dispute that adopting its proposed construction would both exclude the only exemplary treatment regimen expressly taught in the patents (*i.e.*, continuous intravenous administration via an IV drip) and render claim 16 of the '526 patent superfluous. Instead, Eagle argues that the Court nevertheless has no choice but to adopt its construction, because there is no other possible way to read the disputed claims in a consistent manner, and the Court is not free to re-write them.[37] Eagle is wrong.

As just explained, reading the disputed claims as encompassing administration of "the" recited vasopressin compositions, in either diluted or undiluted form, is not only one possible way to read the claims, it is both the most natural way to read them and the way that they would be read by persons knowledgeable about the use and administration of vasopressin.

With respect to dependent claim 16 of the '526 patent, Eagle's citations to *Baxalta Inc. v. Genentech, Inc.*, No. 17-509-TBD, 2018 WL 6304351 (D. Del. Dec.

[37] Indeed, Eagle doubles-down on this argument, pointing out that its construction would also render claim 17 of the '526 patent superfluous. *See supra* at 69-71. That simply adds fuel to the fire, however, and provides further evidence as to why the Court should reject Eagle's construction.

3, 2018) and *Enzo Biochem Inc. v. Applera Corp.*, 780 F.3d 1149 (Fed. Cir. 2015) are unavailing. *Baxalta* expressly noted that there is a presumption that independent claims are broader than their dependent claims, but further noted that the presumption is rebuttable. *Id.* at 11. The court then found the presumption rebutted under the circumstances presented, because the intrinsic evidence clearly dictated a contrary construction. *Id.* Likewise, in *Enzo*, the court found that the intrinsic evidence "clearly indicates that the purpose of this invention was directed towards indirect detection, not direct detection," such that the dependent claim's recitation of "direct detection" could not broaden the independent claim. 780 F.3d at 1156.

Here, by contrast, for all of the reasons Par explains, the intrinsic evidence shows just the opposite of Eagle's proposed construction—*i.e.*, that consistent with preferred method of administration taught in the specification, the patentees intended that the disputed "administering" steps would include, rather than exclude, continuous intravenous administration of the recited vasopressin compositions via an IV drip. *See also, e.g.,* Ex. 3 ('526 patent) at 12:44-45 ("***[a]ny formulation described herein*** can be diluted prior to administration to a subject") (emphasis added).

d. Claim Differentiation Does Not Support Eagle's Construction

Eagle's second argument is the doctrine of claim differentiation compels the Court to adopt its construction, because "[u]nder Par's proposed construction, the

dilution limitations of the '239 patent . . . would be improperly rendered superfluous." *Supra* at 68. That argument misstates Par's position. As Par has repeatedly made clear, under its proposed ordinary meaning construction, the disputed "administering" steps would encompass administering the recited vasopressin compositions via either an IV drip or an IV push (among other possibilities). In other words, Par contends that those claims cover "administering" the vasopressin compositions either with or without dilution. Thus, under Par's construction, the dilution limitations of claim 1 of the '239 patent are not superfluous, they serve to narrow that claim as compared the others—*i.e.*, whereas dilution is required for the '239 patents claims, it is permitted, but optional, for the rest.[38]

[38] Eagle asserts that the dilution steps "were ***dispositive*** to Par's overcoming the Patent Office's obviousness rejection" with respect to the '239 patent. *Supra* at 68 (emphasis in original). That is false. To the contrary, in response to the arguments Par made in the submission cited by Eagle (Ex. 10), the examiner agreed with Par that neither of the references on which he had based his prior rejection (the Treschan and Pharmaceutical Partners of Canada references) "teach a step of diluting the unit dosage in a diluent …," but he nevertheless found that dilution was obvious in view of three other, newly-cited references (Russell, Buck and Young). Ex. 36 (11/22/16 Office Action) at 7. Accordingly, the examiner maintained his obviousness rejection. *Id.* at 14. In reply, the patentees further amended their claims by, among other things, reciting a specific pH range. Ex. 12 (5/22/17 Response to Office Action at 2. It was then that the examiner allowed the claims, finding that the patentees had established "the criticality of the claimed pH range." Ex. 37 (Notice of Allowability) at 2. Thus, it was the claimed pH range, among other things, that was dispositive in the Patent Office allowing the claims, ***not*** the dilution limitations as Eagle falsely asserts.

The only case cited by Eagle—*Chrimar Holding Company, LLC v. ALE USA Inc.*, 732 Fed.Appx. 876 (Fed. Cir. 2018)—supports Par, not Eagle. There, the Federal Circuit noted that "[i]t is hardly unknown for one set of claims to use language that picks out one among several embodiments, especially where other claims (perhaps in the same or related patents) claim more broadly or focus on other embodiments." *Id.* at 884. That is the situation we have here—claim 1 of the '239 patent focuses on the preferred IV drip embodiment and specifically recites a dilution step, while other claims in the related patents more broadly claim administering the recited vasopressin compositions with or without dilution.

e. Eagle's Specification-Based Arguments Are Unavailing

Eagle argues that there is nothing in the specifications that teaches that dilution is "desirable," "necessary," or "even typical." *Supra* at 72-73. Yet, Eagle does not dispute that administering the claimed vasopressin compositions in diluted form is the only form of administration described in the section of the specification entitled "Illustrative Regimen for Therapeutic Use of Vasopressin Formulation." Ex. 1 ('239 patent) at 22:18-67. Nor does Eagle point to anything in the specification that specifically teaches administering the claimed vasopressin via an IV push or other form of direct injection. Moreover, Eagle's assertion ignores, and its proposed construction is inconsistent with, the express teaching in the specification that "***[a]ny***

formulation described herein can be diluted prior to administration to a subject." Ex. 3 ('526 patent) at 12:44-45 (emphasis added).

Thus, while the specification does include many embodiments that broadly describe "administering" the vasopressin to a patient without mentioning dilution, and thereby encompasses administering it in either diluted or undiluted form, there can be no doubt that continuous intravenous infusion via an IV drip is the preferred method of administration taught in the patents.

Eagle cites no basis, in the specification or otherwise, for concluding that the patentees intended to exclude from the claims their preferred, exemplary method of administration, which Dr. Coralic confirms is and was the most common method of administering vasopressin compositions at the time. Coralic Decl. (Ex. 20), ¶ 22. Excluding dilution would not have benefited them in any way, as it would not have distinguished those claims from the prior art. Given that, why would they have excluded from the scope of their claims the most common way by far of administering vasopressin? Eagle's arguments make no practical sense.

Eagle's citation of *Aptalis Pharmatech, Inc. v. Apotex Inc.*, 718 Fed.Appx. 965 (Fed. Cir. 2018) is perplexing. *Supra* at 73. There, the court construed the claimed "coating," which was recited as "surrounding" the active-containing core of extended release beads, as requiring a "continuous" outer film. *Id.* at 969-970. It did so because that was what was taught in "every embodiment in the specification,"

and because the specification distinguished the claimed invention from a prior art reference that it described as having a non-continuous coating. *Id.* So, *Aptalis* supports the conclusion that the claims of the patents-in-suit here should be construed as encompassing the only exemplary treatment regimen expressly taught in the specification (which involves dilution), not precluding it. Thus, *Aptalis* counsels that the Court should reject Eagle's construction rather than adopt it.

f. Eagle Mischaracterizes the Prosecution History

Eagle's prosecution history arguments (*supra*, Section II.C.2.c) are also misguided. Eagle argues that Par's current arguments are inconsistent with those it made during prosecution, but in doing so, mischaracterizes what Par actually said during prosecution. More fundamentally, Eagle points to nothing in the prosecution history that in any way purports to ***exclude*** dilution from any of the claims, which is what is relevant here.

Par's prosecution history statements are not inconsistent with its current claim construction arguments. Eagle points to Par's assertions during prosecution that two prior art references (the Treschan and PPC references) did not teach the dilution steps required by the patent claims being examined at that time, because those references made no mention of dilution. That seems like a pretty unremarkable proposition. Part of the obviousness analysis is to identify differences between the scope and content of the prior art and the claimed invention. Thus, if a claim requires

dilution and a prior art reference does not mention dilution, then that is a difference between the two. Indeed, in responding to the patentees argument, the examiner agreed with them that "neither Treschan nor [PPC] teach a step of diluting the unit dose form in a diluent . . ." Ex. 36 at 7.

Moreover, the patentees did not argue that the claims were not obvious based solely only on that difference, as Eagle asserts. To the contrary, in the Office Action Response cited by Eagle (Ex. 10), the patentees argued non-obviousness based on the fact that the cited references did not teach "all limitations of the claims," did not "provide any reasonable expectation of success in arriving at an invention of the claims," and "did not provide motivation to arrive at an invention of the claims," and they also highlighted the unpredictability of the art. *Id*. at 7-11. The patentees identified a variety of differences between the vasopressin prior art cited by the examiner and the claimed inventions, including that they did not teach or suggest "***every element of the claims*** as amended herewith ***at least*** because no reference suggests [a] dilution of a vasopressin formulation prior to administration, [b] storage of a vasopressin formulation at 2-8 ºC, or [c] that the unit dosage form of the vasopressin formulation exhibits less than about 5% degradation after storage at 2-8 ºC." *Id.* at 7. Eagle focuses on the assertion that the cited vasopressin references did not disclose a dilution step, but ignores the rest of what the patentees said and the fact that they argued that the prior art did not disclose the combination of ***all*** of

the claim limitations. Indeed, the final three pages of the patentees' non-obviousness arguments make no mention of dilution at all.[39] *See also supra* n.38 (discussion of further prosecution).

Par's current arguments are not inconsistent with this history.

More fundamentally, however, nothing in the prosecution history cited by Eagle purports to elucidate in any way the proper reading of the disputed "administering" steps, which is the issue before the Court. Eagle does not argue, for example, that the patentees acted as their own lexicographer or that they made a clear or unequivocal disavowal of claim scope with respect to those limitations. *See, e.g.*, *Thorner*, 669 F.3d at 1365. Its arguments have no relevance to the issues the Court has to resolve.

4. Eagle's Sur-Reply Position:

a. The Intrinsic Evidence Confirms "Administering" Does Not Encompass Dilution.

Par concedes—as it must—that "there is no dispute that terms '***the*** pharmaceutical composition' and '***the*** unit dosage form' refer back to the 'pharmaceutical compositions' and 'unit dosage forms' recited in the earlier

[39] Similarly, in the Interview Summary Eagle cites, there was discussion of various ways to narrow the pending claims so as to distinguish them from the art, including not only the addition of a dilution step, but also adding limitations relating to storage time and stability (noting that "the stability of the compounds is a relevant and important part of the claim"). Ex. 9 at 1.

'providing' steps of the disputed claims." Par Reply at 88, n.34. That is, the dosage form "administered" must have the recited properties.

There is no dispute that dilution will ***change*** the recited properties such that what is given to the patient will have ***different*** properties. Par Reply at 87; Ex. 33 (Suppl. Coralic) ¶ 11.

The only dispute, therefore, is whether the patents use "administering" in a way that encompasses dilution. They do not.

This is confirmed by Par's own cited intrinsic evidence: the description of the preferred embodiments. Par points to the Example titled "Illustrative Regimen for Therapeutic Use of a Vasopressin Formulation" as showing the inventors contemplated dilution. But, that Example explicitly states the dosage form was diluted "***prior to*** use." Ex. 1 at 22:40–45. Similarly, the patents state "[a]ny formulation described herein can be diluted ***prior to*** administration." Ex. 3 at 12:44–45. And, in describing the "73 additional exemplary methods…which expressly recite diluting the claimed vasopressin compositions" (Par Opening at 58–59), the patent explicitly teaches steps of "providing a pharmaceutical composition for intravenous administration" having certain properties, "***diluting the*** unit dosage form," and finally "administering ***the diluted unit dosage form*** to the human by intravenous administration." Ex. 3 at 13:28–47:15; Ex. 4 at 13:35–47:20; Ex. 6 at 14:35–48:20. Thus, in the patents' language, any dilution occurs "***prior to***"

administration, and what is ultimately administered is a "***diluted unit dosage form***," not "***the*** unit dosage form." Par has identified no instance where the patents use an "administer" term to cover a separate dilution step.

The inventors knew how to claim dilution. The '239 patent claims closely follow the embodiments in which a dosage form having certain properties is first provided, then diluted, and then administered as a "***diluted*** unit dosage form." Ex. 1, claim 1. In contrast, the claims of the '478, '526, '209, and '223 patents provide only for administration of "***the*** unit dosage form" or "***the*** pharmaceutical composition" having the recited properties. *See* Claim 1 in Exs. 1, 3–4, 6.

Par's cited evidence does not support it. Claim 1 of the '526 patent supports ***Eagle*** as it recites "***the*** pharmaceutical composition" administered is the same one that was "provid[ed]" with the recited properties. Par's assertion that "[t]he recited vasopressin compositions can be 'administered' in a variety of ways," including where "the composition is first diluted in an IV bag before being infused into the patient," is based solely on its extrinsic declaration and made-up hypothetical, divorced from the claim language and patent disclosures. Par Reply at 85–86.

Contrary to Par's hypothetical, in the patent language, the clinician is "provide[d]" with a vial of vasopressin, "dilutes" the unit dosage form, and administers the "***diluted*** unit dosage form." Far from being "nonsensical," Eagle's position is common sense and consistent with the patents' teachings. If "***the***

pharmaceutical composition" with the claimed properties is extracted from the vial, diluted, and infused into the patient's bloodstream, it is the "***diluted*** pharmaceutical composition" that is administered ***not*** "***the*** pharmaceutical composition" originally in the vial.

Par's position is directly contrary to its prosecution statements. Par did much more than simply assert that the prior art "did not ***teach*** the dilution steps required by the patent claims." Par Reply at 96. Rather, Par argued that prior art disclosing a dosage form ***with the same properties*** to ***achieve the same dosage rate*** did not even "***suggest***" dilution.[40] Eagle Answering at 77–78. Par's current position that a POSA would immediately recognize that the claimed compositions should be diluted, and this was "the most common way by far of administering vasopressin" (Par Reply at 95) cannot be reconciled.

b. Par's Position Violates Claim Construction Canons.

It is Par's position that violates well-established claim construction canons, including that courts must "construe claims with an eye toward giving effect to all of their terms." *Haemonetics*, 607 F.3d at 781. And, contrary to Par's assertion, Eagle ***does*** dispute that its claim construction "would both exclude the only

[40] That Par cited multiple grounds for distinguishing the prior art (Par Reply at 96–98) "does not immunize each of them from being used to construe the claim language." *Andersen*, 474 F.3d at 1374.

exemplary treatment regimen expressly taught in the patents…and render claim 16 of the '526 patent superfluous." Par Reply at 91.

Par concedes that the patents disclose methods of using the claimed formulations in both diluted and undiluted form. Par Opening at 58–59 n.27. "[W]here the patent describes multiple embodiments, every claim does not need to cover every embodiment." *Pacing Techs.*, 778 F.3d at 1026. Par chose to claim a method involving dilution in the '239 patent, but left the '478, '526, '209, and '223 patents to "focus on other embodiments," *i.e.*, administering undiluted compositions. *See Chrimar*, 732 F. App'x at 884.

With respect to claims 16 and 17 of the '526 patent, Par acknowledges that the "presumption that independent claims are broader than their dependent claims…is rebuttable" where "the intrinsic evidence clearly dictated a contrary construction." Par Reply at 92. That is the case here, where the patents' teachings make clear that "administering ***the*** pharmaceutical composition" refers to the composition with the recited properties, and not diluted compositions.

c. Par's "Practical Sense" Argument Is Unavailing

Absent support in the intrinsic evidence, Par resorts to questioning why the applicants would have "excluded from the scope of their claims the most common way by far of administering vasopressin." Par Reply at 95. But the intrinsic record cannot be trumped by hypothetical assumptions about what "makes practical sense"

(*id.*) or what benefits Par might enjoy if it drafted its claims differently. *See Haemonetics*, 607 F.3d at 776; *cf. Chef Am.*, 358 F.3d at 1374. In any event, no "nonsensical" result would occur here, where Par admits the patents contemplate both diluted and undiluted formulations. *See supra*.

d. Eagle's Notice Letter Is Irrelevant

Finally, Par's reliance on Eagle's Notice Letters is unavailing. "ANDA filers are not limited to the theories raised in their paragraph IV letters." *Abbott Labs. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (collecting cases). And there is nothing inconsistent between Eagle's invalidity and claim construction positions. As Eagle made clear in its invalidity contentions, it was apparent that Par would incorrectly argue these claims permit dilution before administration. Ex. 50 (Eagle's Initial Invalidity Contentions) at 67 n.8, 70–71, 75 n.9, 80, 87 n.10, 103 n.11, 107–109. Thus, Eagle appropriately presented invalidity contentions based on Par's apparent claim reading. There is nothing wrong with this approach, nor can Eagle's contentions be viewed as admissions. *See, e.g.*, *Lam Research Corp. v. Schunk Semiconductor*, 65 F. Supp. 3d 863, 870–72 (N.D. Cal. 2014) ("Lam has not cited any case in which a court deemed statements of claim construction by a potential infringer (either in a claim construction brief or in invalidity contentions) to be a 'judicial admission.'").

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ATTACHMENT A

TABLE 1 OF THE PATENTS-IN-SUIT

TABLE 1

Name	Sequence	SEQ ID NO.
Vasopressin (AVP; arginine vasopressin)	CYFQNCPRG-NH_2	1
Gly9-vasopressin (Gly9-AVP)	CYFQNCPRG	2
Asp5-vasopressin (Asp5-AVP)	CYFQDCPRG-NH_2	3
Glu4-vasopressin (Glu4-AVP)	CYFENCPRG-NH_2	4
Glu4Gly9-vasopressin (Glu4Gly9-AVP)	CYFENCPRG	5
AcetylAsp5-vasopressin (AcetylAsp5-AVP)	Ac-CYFQDCPRG-NH_2	6
Acetyl-vasopressin (Acetyl-AVP)	Ac-CYFQNCPRG-NH_2	7
His2-vasopressin (His2-AVP)	CHFQNCPRG-NH_2	8
Leu7-vasopressin (Leu7-AVP)	CYFQNCLRG-NH_2	9
D-Asn-vasopressin (DAsn-AVP)	CYFQ(D-Asn)CPRG-NH_2	10
D-Cys1-vasopressin	(D-Cys)YFQNCPRG-NH_2	11
D-Tyr-vasopressin	C(D-Tyr)FQNCPRG-NH_2	12
D-Phe-vasopressin	CY(D-Phe)QNCPRG-NH_2	13
D-Gln-vasopressin	CYF(D-Gln)NCPRG-NH_2	14
D-Cys6-vasopressin	CYFQN(D-cys)PRG-NH_2	15
D-Pro-vasopressin	CYFQNC(D-pro)RG-NH_2	16
D-Arg-vasopressin	CYFQNCP(D-Arg)G-NH_2	17

CERTIFICATION OF COMPLIANCE

Pursuant to paragraph 9 of the Court's Scheduling Order (D.I. 20) the undersigned hereby certify that this brief complies with the type and number limitations of the Scheduling Order.

Dated: May 3, 2019

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